A Harris
627694

FILE 'REGISTRY' ENTERED AT 15:39:20 ON 04 OCT 2001
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STRUCTURE FILE UPDATES: 3 OCT 2001 HIGHEST RN 360042-01-9
DICTIONARY FILE UPDATES: 3 OCT 2001 HIGHEST RN 360042-01-9

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

```
=> e "tyrosine-related protein-1"/cn 5
E1            1     TYROSINE-PYRUVATE AMINOTRANSFERASE/CN
E2            1     TYROSINE-REGULATED PROTEIN KINASE/CN
E3            0 --> TYROSINE-RELATED PROTEIN-1/CN
E4            1     TYROSINE-SPECIFIC PROTEIN KINASE/CN
E5            1     TYROSINE-SPECIFIC PROTEIN PHOSPHATASE/CN

=> e "trp-1:tyrosine-related protein-1"/cn
E1            1     TRP-.GAMMA.-TERT-BUTYL-GLU-ALA-GLY PENTACHLOROPHENYL ESTER H
                    YDROCHLORIDE/CN
E2            1     TRP-185 LIKE PROTEIN (ARABIDOPSIS THALIANA CLONE COSMID YUP2
                    4F4.IB13H3/G3845 GENE DL4840C)/CN
E3            0 --> TRP-1:TYROSINE-RELATED PROTEIN-1/CN
E4            1     TRP-2 (TYROSINASE-RELATED PROTEIN 2) (CANIS FAMILIARIS EXONS
                     2-3 FRAGMENT)/CN
E5            1     TRP-ALA-GLY-GLY/CN
E6            1     TRP-ARG-D-PHE-ARG-D-TRP-SER-LYS-PRO-VAL-NH2/CN
E7            1     TRP-ARG-PHE-D-ARG-D-TRP-SER-LYS-PRO-VAL-NH2/CN
E8            1     TRP-ARG-PHE-D-ARG-TRP-SER-LYS-PRO-VAL-NH2/CN
E9            1     TRP-ASP REPEATS CONTAINING PROTEIN (SCHIZOSACCHAROMYCES POMB
                    E CLONE A213 GENE SPAC18B11.10 FRAGMENT)/CN
E10           1     TRP-GLY-GLY-PHE-MET/CN
E11           1     TRP-P 1/CN
E12           1     TRP-P 2/CN

=> e "trp-1 tyrosinase-related protein-1"/cn
E1            1     TRP REPRESSOR-BINDING PROTEIN (VIBRIO CHOLERAE STRAIN N16961
                     GENE VC2166)/CN
E2            1     TRP-.GAMMA.-TERT-BUTYL-GLU-ALA-GLY PENTACHLOROPHENYL ESTER H
                    YDROCHLORIDE/CN
E3            0 --> TRP-1 TYROSINASE-RELATED PROTEIN-1/CN
```

```
E4            1     TRP-185 LIKE PROTEIN (ARABIDOPSIS THALIANA CLONE COSMID YUP2
                    4F4.IB13H3/G3845 GENE DL4840C)/CN
E5            1     TRP-2 (TYROSINASE-RELATED PROTEIN 2) (CANIS FAMILIARIS EXONS
                     2-3 FRAGMENT)/CN
E6            1     TRP-ALA-GLY-GLY/CN
E7            1     TRP-ARG-D-PHE-ARG-D-TRP-SER-LYS-PRO-VAL-NH2/CN
E8            1     TRP-ARG-PHE-D-ARG-D-TRP-SER-LYS-PRO-VAL-NH2/CN
E9            1     TRP-ARG-PHE-D-ARG-TRP-SER-LYS-PRO-VAL-NH2/CN
E10           1     TRP-ASP REPEATS CONTAINING PROTEIN (SCHIZOSACCHAROMYCES POMB
                    E CLONE A213 GENE SPAC18B11.10 FRAGMENT)/CN
E11           1     TRP-GLY-GLY-PHE-MET/CN
E12           1     TRP-P 1/CN

=> fil medlin;e human melanocytes/ct 5
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.93     839.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                     0.00     -44.69

FILE 'MEDLINE' ENTERED AT 15:40:54 ON 04 OCT 2001

 FILE LAST UPDATED: 3 OCT 2001 (20011003/UP).  FILE COVERS 1958 TO DATE.

 On April 22, 2001, MEDLINE was reloaded.  See HELP RLOAD for details.

 MEDLINE now contains IN-PROCESS records.  See HELP CONTENT for details.

 MEDLINE is now updated 4 times per week.  A new current-awareness alert
 frequency (EVERYUPDATE) is available.  See HELP UPDATE for more information.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2001 vocabulary.  Enter HELP THESAURUS for details.

 The OLDMEDLINE file segment now contains data from 1958 through 1965.
 Enter HELP CONTENT for details.

 Left, right, and simultaneous left and right truncation are available in the
 Basic Index.  See HELP SFIELDS for details.

 THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE
 SUBSTANCE IDENTIFICATION.


E#    FREQUENCY     AT      TERM
--    ---------     --      ----
E1            0      2      HUMAN LIGHT CHAIN PROTEIN MOIETY REDUCED OF COMPLEMENT
                             FACTOR I/CT
E2            0      1      HUMAN LYMPHOCYTE PROTEIN MOIETY REDUCED/CT
E3            0        --> HUMAN MELANOCYTES/CT
E4            0      1      HUMAN MENOPAUSAL/CT
E5            0      2      HUMAN MENOPAUSAL GONADOTROPINS/CT

=> e human differentiation antigen/ct 5
E#    FREQUENCY     AT      TERM
--    ---------     --      ----
E1         1188     11      HUMAN DEVELOPMENT/CT
E2            0      2      HUMAN DEVELOPMENTS/CT
E3            0        --> HUMAN DIFFERENTIATION ANTIGEN/CT
E4            0      1      HUMAN DONOR/CT
E5            0      1      HUMAN ENDOGENOUS/CT

=> e gp75/ct 5
```

```
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E1           0     2     GP68, GLYCOPROTEIN/CT
E2           0     1     GP70/CT
E3           0     1 --> GP75/CT
E4           0     2     GP75 NGFR/CT
E5           0     1     GP80/CT

=> e e3+all/ct
E1           0   -->   gp75/CT
*********  END***

=> e "trp-2"/ct 5
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E1           0     2     TRP TRNA LIGASE/CT
E2           0     1     TRP(6)-/CT
E3           0       --> TRP-2/CT
E4           0     2     TRP-ALA-GLY-GLY-ASP-ALA-SER-GLY-GLU/CT
E5           0     1     TRP-TRNA/CT

=> e "trp(2)"/ct 5
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E1           0     2     TRP TRANSFER RNA/CT
E2           0     2     TRP TRNA LIGASE/CT
E3           0       --> TRP(2)/CT
E4           0     1     TRP(6)-/CT
E5           0     2     TRP-ALA-GLY-GLY-ASP-ALA-SER-GLY-GLU/CT

=> e human prostate cell/ct 5
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E1           0     2     HUMAN PROJECT, VISIBLE/CT
E2           0     2     HUMAN PROJECTS, VISIBLE/CT
E3           0       --> HUMAN PROSTATE CELL/CT
E4           0     1     HUMAN REDUCED/CT
E5           0     1     HUMAN REPRODUCTIVE/CT

=> e prostate specific membrane antigen/ct 5
E#   FREQUENCY    AT     TERM
--   ---------    --     ----
E1           0     2     PROSTATE SPECIFIC ANTIGEN/CT
E2           0     2     PROSTATE SPECIFIC KALLIKREIN/CT
E3           0       --> PROSTATE SPECIFIC MEMBRANE ANTIGEN/CT
E4           0     2     PROSTATE TRANSURETHRAL RESECTION/CT
E5           0     2     PROSTATE TRANSURETHRAL RESECTIONS/CT

=> e e1+all/ct
E1           0   -->   Prostate Specific Antigen/CT
E2        6075    USE   Prostate-Specific Antigen/CT
*********  END***

=> fil medline,biosis,caplus,biotechno,wpids,jicst
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                 0.90     839.94

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                   ENTRY    SESSION
CA SUBSCRIBER PRICE                                 0.00     -44.69

FILE 'MEDLINE' ENTERED AT 15:42:45 ON 04 OCT 2001

FILE 'BIOSIS' ENTERED AT 15:42:45 ON 04 OCT 2001
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FILE 'JICST-EPLUS' ENTERED AT 15:42:45 ON 04 OCT 2001
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=> s (trp 1 or tyrosin? relate? protein 1)
L1          294 FILE MEDLINE
L2          471 FILE BIOSIS
L3          370 FILE CAPLUS
L4          152 FILE BIOTECHNO
L5           48 FILE WPIDS
L6           27 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L7         1362 (TRP 1 OR TYROSIN? RELATE? PROTEIN 1)

=> s houghton, a?/au,in or houghton a?/au,in
'IN' IS NOT A VALID FIELD CODE
L8          273 FILE MEDLINE
L9          341 FILE BIOSIS
L10         207 FILE CAPLUS
'IN' IS NOT A VALID FIELD CODE
L11          78 FILE BIOTECHNO
L12          34 FILE WPIDS
L13           1 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L14         934 HOUGHTON, A?/AU,IN OR HOUGHTON A?/AU,IN

=> s naftzger, c?/au,in or naftzger c?/au,in
'IN' IS NOT A VALID FIELD CODE
L15           6 FILE MEDLINE
L16           9 FILE BIOSIS
L17           5 FILE CAPLUS
'IN' IS NOT A VALID FIELD CODE
L18           2 FILE BIOTECHNO
L19           1 FILE WPIDS
L20           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L21          23 NAFTZGER, C?/AU,IN OR NAFTZGER C?/AU,IN

=> s sataluri, v?/au,in or sataluri v?/au,in;s gregor, p?/au,in or gregor p?/au,in
'IN' IS NOT A VALID FIELD CODE
L22           0 FILE MEDLINE
L23           0 FILE BIOSIS
L24           0 FILE CAPLUS
'IN' IS NOT A VALID FIELD CODE
L25           0 FILE BIOTECHNO
L26           0 FILE WPIDS
L27           0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L28           0 SATALURI, V?/AU,IN OR SATALURI V?/AU,IN
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'IN' IS NOT A VALID FIELD CODE
L29 144 FILE MEDLINE
L30 101 FILE BIOSIS
L31 61 FILE CAPLUS
'IN' IS NOT A VALID FIELD CODE
L32 29 FILE BIOTECHNO
L33 32 FILE WPIDS
L34 2 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L35 369 GREGOR, P?/AU,IN OR GREGOR P?/AU,IN

=> s l14 and l21 and l35
L36 0 FILE MEDLINE
L37 0 FILE BIOSIS
L38 0 FILE CAPLUS
L39 0 FILE BIOTECHNO
L40 0 FILE WPIDS
L41 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L42 0 L14 AND L21 AND L35

=> s (l14 or l21 or l35) and l7
L43 11 FILE MEDLINE
L44 9 FILE BIOSIS
L45 11 FILE CAPLUS
L46 7 FILE BIOTECHNO
L47 0 FILE WPIDS
L48 0 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L49 38 (L14 OR L21 OR L35) AND L7

=> dup rem l49
PROCESSING COMPLETED FOR L49
L50 15 DUP REM L49 (23 DUPLICATES REMOVED)

=> d 1-15 cbib abs;s l7 and (insect cell line or human differ? antigen or human melanocyte? or gp75 or gp100 or trp 2 or human prostate cell or prostate specific membrane antigen)

L50 ANSWER 1 OF 15 MEDLINE DUPLICATE 1
2001349695 Document Number: 21305988. PubMed ID: 11412044. Diverse roles of conserved asparagine-linked glycan sites on tyrosinase family glycoproteins. Xu Y; Bartido S; Setaluri V; Qin J; Yang G; **Houghton A N.** (The Swim Across America Laboratory, The Weill Graduate School of Medical Sciences of Cornell University, New York, New York 10021, USA.) EXPERIMENTAL CELL RESEARCH, (2001 Jul 1) 267 (1) 115-25. Journal code: EPB; 0373226. ISSN: 0014-4827. Pub, country: United States. Language: English.

AB The tyrosinase family of genes has been conserved throughout vertebrate evolution. The role of conserved N-glycan sites in sorting, stability, and activity of tyrosinase family proteins was investigated using two family members from two different species, mouse gp75/tyrosinase-related protein (**TRP**)-**1**/Tyrp1 and human tyrosinase. Potential N-linked glycosylation sites on the lumenal domains of mouse gp75/**TRP**-**1**/Tyrp1 and human tyrosinase were eliminated by site-directed mutagenesis (Asn to Gln substitutions). Our results show that selected conserved N-glycan sites on tyrosinase family members are crucial for stability in the secretory pathway and endocytic compartment and for enzymatic activity. Different glycan sites on the same tyrosinase family polypeptide can perform distinct functions, and conserved sites on

tyrosinase family paralogues can perform different functions. Copyright 2001 Academic Press.

L50 ANSWER 2 OF 15 MEDLINE DUPLICATE 2

2000040370 Document Number: 20040370. PubMed ID: 10570265. A role for a melanosome transport signal in accessing the MHC class II presentation pathway and in eliciting CD4+ T cell responses. Wang S; Bartido S; Yang G; Qin J; Moroi Y; Panageas K S; Lewis J J; **Houghton A N.** (Swim Across America Laboratory, Department of Surgery, Cornell University Graduate School of Medical Sciences, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.) JOURNAL OF IMMUNOLOGY, (1999 Dec 1) 163 (11) 5820-6. Journal code: IFB; 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Melanosomal membrane proteins are frequently recognized by the immune system of patients with melanoma and vitiligo. Melanosomal glycoproteins are transported to melanosomes by a dileucine-based melanosomal transport signal (MTS). To investigate whether this sorting signal could be involved in presentation of melanosome membrane proteins to the immune system, we devised a fusion construct containing the MTS from the mouse brown locus product gp75/**tyrosinase-related protein-1** and full-length OVA as a reporter Ag. The fusion protein was expressed as an intracellular membrane protein, sorted to the endocytic pathway, processed, and presented by class II MHC molecules. DNA immunization with this construct elicited CD4+ T cell proliferative responses in vivo. Ag presentation and T cell responses in vitro and in vivo required a functional MTS. Mutations of either the upstream leucine in MTS or elimination of the entire MTS negated in vitro Ag presentation and in vivo T cell responses. In a mouse melanoma model, DNA immunization with MTS constructs protected mice from tumor challenge in a CD4+ T cell-dependent manner, but complete deletion of MTS decreased tumor rejection. Therefore, MTS can target epitopes to the endocytic pathway leading to presentation by class II MHC molecules to helper T cells.

L50 ANSWER 3 OF 15 MEDLINE

2000054512 Document Number: 20054512. PubMed ID: 10587362. Coupling and uncoupling of tumor immunity and autoimmunity. Bowne W B; Srinivasan R; Wolchok J D; Hawkins W G; Blachere N E; Dyall R; Lewis J J; **Houghton A N.** (Memorial Sloan-Kettering Cancer Center, New York, New York 10021, USA.) JOURNAL OF EXPERIMENTAL MEDICINE, (1999 Dec 6) 190 (11) 1717-22. Journal code: I2V; 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.

AB Self-antigens, in the form of differentiation antigens, are commonly recognized by the immune system on melanoma and other cancers. We have shown previously that active immunization of mice against the melanocyte differentiation antigen, a tyrosinase-related protein (TRP) gp75(**TRP-1**) (the brown locus protein) expressed by melanomas, could induce tumor immunity and autoimmunity manifested as depigmentation. In this system, tumor immunity and autoimmunity were mediated by autoantibodies. Here, we characterize immunity against another tyrosinase family glycoprotein TRP-2 (the slaty locus protein), using the same mouse model and method of immunization. As observed previously for gp75(**TRP-1**), immunity was induced by DNA immunization against a xenogeneic form of TRP-2, but not against the syngeneic gene, and depended on CD4(+) cells. Immunization against TRP-2 induced autoantibodies and autoreactive cytotoxic T cells. In contrast to immunization against gp75(**TRP-1**), both tumor immunity and autoimmunity required CD8(+) T cells, but not antibodies. Only autoimmunity required perforin, whereas tumor immunity proceeded in the absence of perforin. Thus, immunity induced against two closely related autoantigens that are highly conserved throughout vertebrate evolution involved qualitatively different mechanisms, i.e., antibody versus CD8(+) T cell. However, both pathways led to tumor immunity and identical phenotypic manifestations of autoimmunity.

L50 ANSWER 4 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

1999:188310 Document No.: PREV199900188310. MHC class I processing of a misfolded transmembrane protein by a proteasome-independent pathway. Qin, J.; Xu, Y.; Moroi, Y.; Setaluri, V.; **Houghton, A. N.**. Sloan-Kettering Div., Cornell Univ. Graduate Sch. Med. Sciences, Memorial Sloan-Kettering Cancer Cent., New York, NY 10021 USA. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 471. Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research. ISSN: 0197-016X. Language: English.

L50 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2001 ACS

2000:431795 Document No. 134:84768 Injection of DNA encoding granulocyte-macrophage colony-stimulating factor recruits dendritic cells for immune adjuvant effects. Bowne, Wilbur B.; Wolchok, Jedd D.; Hawkins, William G.; Srinivasan, Roopa; **Gregor, Polly**; Blachere, Nathalie E.; Moroi, Yoichi; Engelhorn, Manuel E.; **Houghton, Alan N.**; Lewis, Jonathan J. (Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA). Cytokines, Cell. Mol. Ther., 5(4), 217-225 (English) 1999. CODEN: CCMTFO. ISSN: 1368-4736. Publisher: Martin Dunitz Ltd..

AB An important issue for effective vaccines is the development of potent adjuvants that can facilitate induction or augmentation of immunity. Granulocyte-macrophage colony-stimulating factor (GM-CSF) is a growth factor for myeloid progenitors of monocytes and dendritic cells (DC), which upon maturation are antigen-presenting cells (APC). The adjuvant effects of inoculation of DNA encoding GM-CSF into skin were studied. Initial expts. examd. whether the GM-CSF gene injected into the skin of mice could affect the d. of epidermal DC (Langerhans cells). DNA encoding GM-CSF delivered by particle bombardment into skin resulted in a significant increase of epidermal DC at the inoculation site. Kinetic anal. of epidermal recruitment after GM-CSF inoculation showed an increase in DC that peaked at seven days. This increase was accompanied by recruitment of DC into draining lymph nodes. The adjuvant effects of DNA encoding GM-CSF inoculated into skin were measured by the ability to augment antibody and T-cell responses against poorly immunogenic tumor antigens. Peptide immunization at skin sites contg. epidermal DC newly recruited by GM-CSF DNA elicited T-cell responses against mutant p53, whereas peptide immunization of control skin sites did not elicit any detectable T-cell responses. Likewise, generation of antibodies following immunization with DNA encoding human gp75TRP1, a tyrosinase family member expressed by melanomas, was accelerated and protection from tumor challenge augmented by GM-CSF DNA.

L50 ANSWER 6 OF 15 BIOSIS COPYRIGHT 2001 BIOSIS

1999:184406 Document No.: PREV199900184406. IFN-gamma inhibits the antibody response to syngeneic gp75/**tyrosinase related protein-1** induced by DNA immunization with xenogeneic gp75. Wolchok, J. D.; Srinivasan, R.; Bowne, W. B.; Moroi, Y.; Lewis, J. J.; **Houghton, A. N.**. Memorial Sloan-Kettering Cancer Center, New York, NY 10021 USA. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 1999) Vol. 40, pp. 75. Meeting Info.: 90th Annual Meeting of the American Association for Cancer Research Philadelphia, Pennsylvania, USA April 10-14, 1999 American Association for Cancer Research. ISSN: 0197-016X. Language: English.

L50 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2001 ACS

1998:717534 Document No. 130:80094 Heteroclitic immunization induces tumor immunity. Dyall, Ruben; Bowne, Wilbur B.; Weber, Lawrence W.; LeMaoult, Joel; Szabo, Paul; Moroi, Yoichi; Piskun, Gregory; Lewis, Jonathan J.; **Houghton, Alan N.**; Nikolic-Zugic, Janko (T Cell Development Laboratory, Immunology Program, Memorial Sloan-Kettering Cancer Center, New York, NY, 10021, USA). J. Exp. Med., 188(9), 1553-1561 (English) 1998. CODEN: JEMEAV. ISSN: 0022-1007. Publisher: Rockefeller University Press.

AB In tumor transplantation models in mice, cytotoxic T lymphocytes (CTLs)

are typically the primary effector cells. CTLs recognize major histocompatibility complex (MHC) class I-assocd. peptides expressed by tumors, leading to tumor rejection. Peptides presented by cancer cells can originate from viral proteins, normal self-proteins regulated during differentiation, or altered proteins derived from genetic alterations. However, many tumor peptides recognized by CTLs are poor immunogens, unable to induce activation and differentiation of effector CTLs. The authors used MHC binding motifs and the knowledge of class I:peptide:TCR structure to design heteroclitic CTL vaccines that exploit the expression of poorly immunogenic tumor peptides. The in vivo potency of this approach was demonstrated using viral and self-(differentiation) antigens as models. First, a synthetic variant of a viral antigen was expressed as a tumor antigen, and heteroclitic immunization with peptides and DNA was used to protect against tumor challenge and elicit regression of 3-d tumors. Second, a peptide from a relevant self-antigen of the tyrosinase family expressed by melanoma cells was used to design a heteroclitic peptide vaccine that successfully induced tumor protection. These results establish the in vivo applicability of heteroclitic immunization against tumors, including immunity to poorly immunogenic self-proteins.

L50 ANSWER 8 OF 15 MEDLINE DUPLICATE 3

1998411382 Document Number: 98411382. PubMed ID: 9739060. Tumor immunity and autoimmunity induced by immunization with homologous DNA. Weber L W; Bowne W B; Wolchok J D; Srinivasan R; Qin J; Moroi Y; Clynes R; Song P; Lewis J J; **Houghton A N.** (The Swim Across America Laboratory, Sloan-Kettering Division, Cornell University Graduate School of Medical Sciences, New York 10021, USA.) JOURNAL OF CLINICAL INVESTIGATION, (1998 Sep 15) 102 (6) 1258-64. Journal code: HS7; 7802877. ISSN: 0021-9738. Pub. country: United States. Language: English.

AB The immune system can recognize self antigens expressed by cancer cells. Differentiation antigens are prototypes of these self antigens, being expressed by cancer cells and their normal cell counterparts. The tyrosinase family proteins are well characterized differentiation antigens recognized by antibodies and T cells of patients with melanoma. However, immune tolerance may prevent immunity directed against these antigens. Immunity to the brown locus protein, gp75/ **tyrosinase-related protein-1**, was investigated in a syngeneic mouse model. C57BL/6 mice, which are tolerant to gp75, generated autoantibodies against gp75 after immunization with DNA encoding human gp75 but not syngeneic mouse gp75. Priming with human gp75 DNA broke tolerance to mouse gp75. Immunity against mouse gp75 provided significant tumor protection. Manifestations of autoimmunity were observed, characterized by coat depigmentation. Rejection of tumor challenge required CD4(+) and NK1.1(+) cells and Fc receptor gamma-chain, but depigmentation did not require these components. Thus, immunization with homologous DNA broke tolerance against mouse gp75, possibly by providing help from CD4(+) T cells. Mechanisms required for tumor protection were not necessary for autoimmunity, demonstrating that tumor immunity can be uncoupled from autoimmune manifestations.

L50 ANSWER 9 OF 15 MEDLINE DUPLICATE 4

1998200038 Document Number: 98200038. PubMed ID: 9540969. The cytoplasmic tail of the mouse brown locus product determines intracellular stability and export from the endoplasmic reticulum. Xu Y; Vijayasaradhi S; **Houghton A N.** (The Swim Across America Laboratory, Memorial Sloan-Kettering Cancer Center and Sloan-Kettering Division, Cornell University Graduate School of Medical Sciences, New York, New York 10021, USA.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1998 Apr) 110 (4) 324-31. Journal code: IHZ; 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB Several melanosome membrane proteins have been identified, forming a family of proteins known as tyrosinase related proteins. Human **TRP-1**/gp75 is sorted to melanosomes through the endoplasmic reticulum and Golgi complex to the endocytic pathway, directed by a sorting signal located in the cytoplasmic tail. This hexapeptide

cytoplasmic sequence, which is conserved in the tyrosinase related protein family and through vertebrate evolution, was shown to act also as a sorting signal in mouse gp75, confirming that its sorting and cellular retention function is conserved between human and mouse. The cytoplasmic tail influenced the rate and efficiency of intracellular transport of gp75 from the endoplasmic reticulum to the cis-Golgi. Deletion of 33 or 27 amino acids from the carboxyl end of the 38 amino acid cytoplasmic tail of gp75 caused retention and rapid degradation of the truncated gp75 in the endoplasmic reticulum. This defective movement could be fully corrected by extending the truncated tail with the unrelated cytoplasmic tail of the low density lipoprotein receptor. Thus, the cytoplasmic tail of mouse gp75 not only determines sorting to the endocytic/melanosomal compartment, but also controls export from the endoplasmic reticulum to Golgi.

L50 ANSWER 10 OF 15 MEDLINE DUPLICATE 5
97121471 Document Number: 97121471. PubMed ID: 8962137. Immune response to a differentiation antigen induced by altered antigen: a study of tumor rejection and autoimmunity. **Naftzger C**; Takechi Y; Kohda H; Hara I; Vijayasaradhi S; **Houghton A N**. (Swim Across America Laboratory, Memorial Sloan-Kettering Cancer Center, New York, NY 10021, USA.) PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Dec 10) 93 (25) 14809-14. Journal code: PV3; 7505876. ISSN: 0027-8424. Pub. country: United States. Language: English.
AB Recognition of self is emerging as a theme for the immune recognition of human cancer. One question is whether the immune system can actively respond to normal tissue autoantigens expressed by cancer cells. A second but related question is whether immune recognition of tissue autoantigens can actually induce tumor rejection. To address these issues, a mouse model was developed to investigate immune responses to a melanocyte differentiation antigen, **tyrosinase-related protein 1** (or gp75), which is the product of the brown locus. In mice, immunization with purified syngeneic gp75 or syngeneic cells expressing gp75 failed to elicit antibody or cytotoxic T-cell responses to gp75, even when different immune adjuvants and cytokines were included. However, immunization with altered sources of gp75 antigen, in the form of either syngeneic gp75 expressed in insect cells or human gp75, elicited autoantibodies to gp75. Immunized mice rejected metastatic melanomas and developed patchy depigmentation in their coats. These studies support a model of tolerance maintained to a melanocyte differentiation antigen where tolerance can be broken by presenting sources of altered antigen (e.g., homologous xenogeneic protein or protein expressed in insect cells). Immune responses induced with these sources of altered antigen reacted with various processed forms of native, syngeneic protein and could induce both tumor rejection and autoimmunity.

L50 ANSWER 11 OF 15 MEDLINE DUPLICATE 6
96042160 Document Number: 96042160. PubMed ID: 7595233. Implicating a role for immune recognition of self in tumor rejection: passive immunization against the brown locus protein. Hara I; Takechi Y; **Houghton A N**. (Memorial Sloan-Kettering Cancer Center, New York 10021, USA.) JOURNAL OF EXPERIMENTAL MEDICINE, (1995 Nov 1) 182 (5) 1609-14. Journal code: I2V; 2985109R. ISSN: 0022-1007. Pub. country: United States. Language: English.
AB The immune system can recognize differentiation antigens that are selectively expressed on malignant cells and their normal cell counterparts. However, it is uncertain whether immunity to differentiation antigens can effectively lead to tumor rejection. The mouse brown locus protein, gp75 or **tyrosinase-related protein 1**, is a melanocyte differentiation antigen expressed by melanomas and normal melanocytes. The gp75 antigen is recognized by autoantibodies and autoreactive T cells in persons with melanoma. To model autoimmunity against a melanocyte differentiation antigen, mouse antibodies against gp75 were passively transferred into tumor-bearing mice. Passive immunization with a mouse monoclonal antibody against gp75 induced protection and rejection of both subcutaneous tumors and lung metastases

in syngeneic C57BL/6 mice, including established tumors. Passive immunity produced coat color alterations but only in regenerating hairs. This system provides a model for autoimmune vitiligo and shows that immune responses to melanocyte differentiation antigens can influence mouse coat color. Immune recognition of a melanocyte differentiation antigen can reject tumors, providing a basis for targeting tissue autoantigens expressed on cancer.

L50 ANSWER 12 OF 15 MEDLINE DUPLICATE 7
95370357 Document Number: 95370357. PubMed ID: 7642699. Intracellular sorting and targeting of melanosomal membrane proteins: identification of signals for sorting of the human brown locus protein, gp75. Vijayasaradhi S; Xu Y; Bouchard B; **Houghton A N.** (Immunology Program, Memorial Sloan-Kettering Cancer Center, New York 10021, USA.) JOURNAL OF CELL BIOLOGY, (1995 Aug) 130 (4) 807-20. Journal code: HMV; 0375356. ISSN: 0021-9525. Pub. country: United States. Language: English.

AB The structural and functional integrity of cytoplasmic organelles is maintained by intracellular mechanisms that sort and target newly synthesized proteins to their appropriate cellular locations. In melanocytic cells, melanin pigment is synthesized in specialized organelles, melanosomes. A family of melanocyte-specific proteins, known as tyrosinase-related proteins that regulate melanin pigment synthesis, is localized to the melanosomal membrane. The human brown locus protein, **tyrosinase-related protein-1** or gp75, is the most abundant glycoprotein in melanocytic cells, and is a prototype for melanosomal membrane proteins. To investigate the signals that allow intracellular retention and sorting of glycoprotein (gp)75, we constructed protein chimeras containing the amino-terminal extracellular domain of the T lymphocyte surface protein CD8, and transmembrane and cytoplasmic domains of gp75. In fibroblast transfectants, chimeric CD8 molecules containing the 36-amino acid cytoplasmic domain of gp75 were retained in cytoplasmic organelles. Signals in the gp75 cytoplasmic tail alone, were sufficient for intracellular retention and targeting of the chimeric proteins to the endosomal/lysosomal compartment. Analysis of subcellular localization of carboxy-terminal deletion mutants of gp75 and the CD8/gp75 chimeras showed that deletion of up amino acids from the gp75 carboxyl terminus did not affect intracellular retention and sorting, whereas both gp75 and CD8/gp75 mutants lacking the carboxyl-terminal 27 amino acids were transported to the cell surface. This region contains the amino acid sequence, asn-gln-pro-leu-leu-thr, and this hexapeptide is conserved among other melanosomal proteins. Further evidence showed that this hexapeptide sequence is necessary for intracellular sorting of gp75 in melanocytic cells, and suggested that a signal for sorting melanosomal proteins along the endosomal/lysosomal pathway lies within this sequence. These data provide evidence for common signals for intracellular sorting of melanosomal and lysosomal proteins, and support the notion that lysosomes and melanosomes share a common endosomal pathway of biogenesis.

L50 ANSWER 13 OF 15 MEDLINE DUPLICATE 8
95341012 Document Number: 95341012. PubMed ID: 7615964. Melanocyte differentiation marker gp75, the brown locus protein, can be regulated independently of tyrosinase and pigmentation. Vijayasaradhi S; Doskoch P M; Wolchok J; **Houghton A N.** (Immunology Program, Memorial Sloan-Kettering Cancer Center, New York, New York, USA.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1995 Jul) 105 (1) 113-9. Journal code: IHZ; 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB Human melanoma arises from epidermal melanocytes and displays remarkable phenotypic heterogeneity. This heterogeneity in part reflects the ability of melanoma cells to undergo differentiation along a pathway parallel to differentiation of normal melanocytes. Tyrosinase, encoded by the albino (c), and the **tyrosinase-related protein-1** or gp75, encoded by the brown (b) locus, are two of the best-characterized markers for melanocyte differentiation. Both molecules are glycoproteins expressed in melanosomes, the site of pigment synthesis. We studied the regulation of these proteins in human melanoma cells

induced by the polar-planar compound hexamethylene bisacetamide (HMBA). In well-differentiated melanoma cell lines, HMBA induced dendritic morphology and specifically regulated the expression of melanosomal glycoproteins (but not a panel of other molecules expressed by melanoma cells). HMBA specifically down-regulated gp75 expression by rapidly decreasing the steady-state level of gp75 mRNA and gp75 synthesis. HMBA was able to down-regulate gp75 expression even in the presence of cholera toxin, which when added alone induced a two- to threefold increase in gp75 expression. In contrast to uniform down-regulation of gp75 expression, HMBA could either up-regulate or down-regulate tyrosinase expression and pigmentation. Based on the differential regulation of gp75 and tyrosinase, melanoma cells could be classified into two groups. In one group, gp75 expression was coordinately regulated with tyrosinase activity and pigmentation. In the other group, gp75 expression and tyrosinase activity and pigmentation were dissociated (with pigmentation coupling to tyrosinase activity, not to gp75 expression). These results show that in mature melanocytic cells, regulation of gp75 expression follows a pattern that can be independent of regulation of tyrosinase and pigmentation.

L50 ANSWER 14 OF 15 MEDLINE DUPLICATE 9
94165508 Document Number: 94165508. PubMed ID: 7509835. Production and characterization of antibodies against human tyrosinase. Bouchard B; Vijayasaradhi S; **Houghton A N.** (Memorial Sloan-Kettering Cancer Center, New York, NY 10021.) JOURNAL OF INVESTIGATIVE DERMATOLOGY, (1994 Mar) 102 (3) 291-5. Journal code: IHZ; 0426720. ISSN: 0022-202X. Pub. country: United States. Language: English.

AB Proteins mapping at different loci are involved in melanogenesis and share several characteristic structural features (b locus, c locus, and slaty locus products). We describe a method to produce specific antibodies against human tyrosinase, the product of the c locus. Mouse L cells transfected with a human tyrosinase cDNA were used to generate antibodies by immunization of syngeneic C3H mice. These antibodies were able to precipitate the tyrosinase glycoprotein from both melanocytic cells and transfectants expressing tyrosinase. In contrast, transfectants expressing the related but distinct b locus protein (gp75 or **TRP-1**) did not react with these antibodies. In most cases, tyrosinase enzymatic activity could be precipitated and recovered in immune complexes, but one antibody response blocked tyrosinase activity. Immunostaining with anti-tyrosinase antibodies revealed an intracellular granular pattern in tyrosinase transfectants and melanocytic cells, but not transfectants expressing the b locus protein. This approach provides a general method to produce specific antibodies against tyrosinase, other members of the tyrosinase family of proteins, and potentially any other differentiation antigen.

L50 ANSWER 15 OF 15 MEDLINE
93378354 Document Number: 93378354. PubMed ID: 8368771. Recognition of autoantigens by patients with melanoma. **Houghton A N;** Vijayasaradhi S; Bouchard B; **Naftzger C;** Hara I; Chapman P B. (Memorial Sloan-Kettering Cancer Center, New York, New York.) ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1993 Aug 12) 690 59-68. Ref: 49. Journal code: 5NM; 7506858. ISSN: 0077-8923. Pub. country: United States. Language: English.

L51	125	FILE MEDLINE
L52	160	FILE BIOSIS
L53	189	FILE CAPLUS
L54	68	FILE BIOTECHNO
L55	12	FILE WPIDS
L56	13	FILE JICST-EPLUS

TOTAL FOR ALL FILES
L57 567 L7 AND (INSECT CELL LINE OR HUMAN DIFFER? ANTIGEN OR HUMAN MELAN

OCYTE? OR GP75 OR GP100 OR TRP 2 OR HUMAN PROSTATE CELL OR PROST
ATE SPECIFIC MEMBRANE ANTIGEN)

=> s l57 and immune response
L58 9 FILE MEDLINE
L59 10 FILE BIOSIS
L60 24 FILE CAPLUS
L61 4 FILE BIOTECHNO
L62 8 FILE WPIDS
L63 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L64 56 L57 AND IMMUNE RESPONSE

=> s (method? or composi?) and l64
L65 2 FILE MEDLINE
L66 6 FILE BIOSIS
L67 11 FILE CAPLUS
L68 0 FILE BIOTECHNO
L69 8 FILE WPIDS
L70 1 FILE JICST-EPLUS

TOTAL FOR ALL FILES
L71 28 (METHOD? OR COMPOSI?) AND L64

=> dup rem l71
PROCESSING COMPLETED FOR L71
L72 19 DUP REM L71 (9 DUPLICATES REMOVED)

=> d 1-19 cbib abs

L72 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 1
2001:507558 Document No. 135:106284 Enhanced **immune response** to a vaccine. Emtage, Peter; Barber, Brian H.; Sambhara, Suryprakash; Sia, Charles Dwo Yuan (Aventis Pasteur Limited, Can.). PCT Int. Appl. WO 2001049317 A2 20010712, 62 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-CA5 20010105. PRIORITY: US 2000-PV174587 20000105.
AB A **method** of enhancing an **immune response** is disclosed. The **method** involves an initial priming of the animal with an inducing agent, subsequently followed by administration of an inducing agent-antigen mixt. The antigen may be a tumor assocd. antigen, pathogenic organism antigen, autoimmune antigen, immunogenic fragment thereof, or a nucleic acid coding therefor.

L72 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 2
2001:319754 Document No. 134:339527 **Method** of inducing and/or enhancing an **immune response** to tumor antigens. Berinstein, Neil; Tartaglia, James; Moingeon, Philippe; Barber, Brian (Aventis Pasteur Limited, Can.). PCT Int. Appl. WO 2001030382 A1 20010503, 60 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION:

WO 2000-CA1253 20001020. PRIORITY: US 1999-PV160879 19991022; US 2000-PV223325 20000807.

AB An improved **method** of inducing and/or enhancing an **immune response** to a tumor antigen is disclosed. The **method** involves administering the tumor antigen, nucleic acid coding therefor, vectors and/or cells comprising said nucleic acid, or vaccines comprising the aforementioned to a lymphatic site.

L72 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 3

2001:300541 Document No. 134:309698 Cancer vaccine using tumor antigen-pulsed antigen-presenting cells and immunostimulants. Mallack, Marc K.; Sivanandham, Muthukumaran (St. Vincent's Hospital and Medical Center of New York, USA). PCT Int. Appl. WO 2001028583 A2 20010426, 54 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US28837 20001018.

AB The invention concerns an immunotherapeutic vaccine providing antigen presenting cells that have been pulsed with a disrupted cell prepn. which includes enucleated cytosol and cell membranes of cancer cells infected with a recombinant vaccinia virus encoding at least one immunostimulating mol. In a preferred embodiment, the vaccine includes autologous dendritic/monocytic cells (DC/M) that present a mixt. of antigens (present in the enucleated cytosol and cell membranes) from melanoma cell lines that have been infected with a recombinant vaccinia virus encoding IL-2. In another of the preferred embodiments, the enucleated cytosol and cell membranes are from melanoma cells harvested from the patient to be treated. A **method** of making the vaccine and **methods** of using the vaccine to stimulate an anti-cancer **immune response** and to treat a patient with a cancer are also described.

L72 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2001 ACS

2001:12285 Document No. 134:99563 HLA binding peptides and their uses. Sette, Alessandro; Sidney, John; Southwood, Scott (Epimmune Inc., USA). PCT Int. Appl. WO 2001000225 A1 20010104, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US17842 20000628. PRIORITY: US 1999-PV141422 19990629.

AB The present invention provides the means and **methods** for selecting immunogenic peptides and the immunogenic peptide **compns** . capable of specifically binding glycoproteins encoded by HLA alleles and inducing T cell activation in T cells restricted by the allele. The peptides are useful to elicit an **immune response** against a desired antigen.

L72 ANSWER 5 OF 19 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

AN 2001-123319 [13] WPIDS

AB WO 200109303 A UPAB: 20010307

NOVELTY - Immunogenic **compositions** comprising Flt-3 ligand encoding polynucleotide and one or more antigen or cytokine encoding polynucleotides, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are provided for:

(1) a **composition** (C1) comprising:

(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide

(N1) which hybridizes, at 42 deg. C in 50% formamide, 5 x SSC (saline sodium chloride), 50 mM sodium phosphate, 5 x Denhardt's solution, 10% dextran sulfate, and 20 micro g/ml denatured, sheared salmon sperm DNA, followed by washing at 65 deg. C in 0. 1 x SSC and 0. 1 % sodium dodecyl sulfate (SDS) (w/v), to a reference nucleic acid having a 839, 852, 1152, 663, 519, 1080, 537, or 859 (S1-S8, respectively) nucleotide sequence defined in the specification, or their complements, where the first polynucleotide encodes a polypeptide having immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of a nucleic acid (N2) comprising a second polynucleotide encoding one or more antigens, or one or more cytokines, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(2) a **composition** (C2) comprising:

(a) 1 ng to 10 mg of a nucleic acid comprising a first polynucleotide (N3) which encodes a first polypeptide which, except for at least one but not more than 20 amino acid substitutions, deletions, or insertions, is identical to a second polypeptide selected from amino acids 28 to 163 of the 231 amino acid sequence (S9), amino acids 27 to 160 of 235 amino acid sequence (S15), or amino acids 27 to 185 of 235 amino acid sequence (S17) (all sequences are defined in the specification), where the first polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(3) a pharmaceutical **composition** (C3) comprising:

(a) 1 ng to 10 mg of a nucleic acid molecule comprising a first polynucleotide (N4) encoding an amino acid sequence that is at least 90%, preferably 97%, identical to a reference amino acid sequence selected from S9, 189 (S10), 220 (S11), 232 (S12), 172 (S14), S15, 178 (S16), S17 or 185 (S18) amino acid sequence defined in the specification, where % identity is determined using the Bestfit program with default parameters, and the polypeptide has immunity-enhancing activity when administered to a vertebrate;

(b) 1 ng to 30 mg of N2, where the first and second polynucleotides are non-infectious and non-integrating, and are operably associated with control sequences which direct their expression;

(4) a **method** (M1) for enhancing an **immune response** in a vertebrate, comprising administering C1, C2 or C3 to a tissue of the vertebrate, where the first and second polynucleotides are expressed in vivo in an amount effective for a polypeptide expressed by the first polynucleotide to enhance the immunogenicity of one or more antigens, or one or more cytokines; and

(5) a **method** (M2) of suppressing tumor growth in a mammal, comprising administering C1, C2 or C3 to a tissue of a mammal.

ACTIVITY - Antirheumatic; antiarthritic; immunostimulant; antiviral; antibacterial; antifungal; antiparasitic; cytostatic; immunosuppressive; protozoacide; antiinflammatory.

Three groups of mice were used in the study. One group (n=9) was co-injected with VR6200 (a Flt-3 ligand-encoding plasmid) and VR1623 (bicistronic chimeric Id vector) (100 micro g each) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection. Control groups (n=10 each) were co-injected with VR1623 and VR1051 (control plasmid), or VR1605 (generic cloning vector comprising the constant regions of human kappa light chain and gamma 1 heavy chain separated by a CITE (cap independent translational enhancer)) or alone (200 micro g) on days 0, 14, and 28, and challenged with 500 38C13 tumor cells two weeks following the last injection.

The co-injection of a Flt-3 ligand-encoding plasmid (100 micro g of VR6200) with a tumor-specific antigen-encoding plasmid (100 micro g of VR1623) significantly enhanced protection from tumor challenge. Eight out of nine mice injected with VR1623 and VR6200 survived the challenge as compared to zero out of ten mice surviving after being immunized with

VR1623 and the control plasmid, VR1051. This increased survival was statistically significant p=0.00007. Furthermore, the co-injection of a Flt-3 ligand-encoding plasmid (VR6200) with an idiotype antigen-encoding plasmid (VR1623) resulted in greatly enhanced anti-Id antibody titer relative to mice injected with VR1623 and VR1051, or with VR1623 alone.

MECHANISM OF ACTION - Vaccine.

USE - The **compositions** are useful for suppressing tumor growth in a mammal. The tumor is melanoma, glioma or lymphoma, particularly B-cell lymphoma. The **compositions** are used in conjunction with additional cancer treatments (claimed).

The immunogenic **compositions** can also be used for the prophylactic and/or therapeutic treatment of:

(a) bacterial (e.g. Bacillus infections), viral (e.g. hepatitis B and C in humans), parasitic (e.g. malaria) and fungal infections;

(b) autoimmune diseases (e.g. rheumatoid arthritis and osteoarthritis);

(c) cancer (e.g. cancers of stomach, small intestine, liver, etc.); and

(d) Aujeszky's disease in pigs.

Various other examples of these diseases are given in the specification.

Dwg.0/9

L72 ANSWER 6 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS

2001:468723 Document No.: PREV200100468723. Development of a novel chimeric protein-based melanoma vaccine. Kang, Xiaoqiang (1); Patel, Dipa (1); Shi, Jack (1); Bassi, Rajiv (1); Balderes, Paul (1); Hooper, Andrea (1); Bohlen, Peter (1); Hicklin, Daniel J. (1). (1) ImClone Systems Incorporated, New York, NY USA. Proceedings of the American Association for Cancer Research Annual Meeting, (March, 2001) Vol. 42, pp. 288. print. Meeting Info.: 92nd Annual Meeting of the American Association for Cancer Research New Orleans, LA, USA March 24-28, 2001 ISSN: 0197-016X. Language: English. Summary Language: English.

L72 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2001 ACS

2000:402017 Document No. 133:54574 Recombinant vectors expressing multiple costimulatory molecules, host cell infection, and uses in immunogenic applications. Schlom, Jeffrey; Hodge, James; Panicali, Dennis (United States Dept. of Health and Human Services, USA; Therion Biologics Corporation). PCT Int. Appl. WO 2000034494 A1 20000615, 188 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US26866 19991112. PRIORITY: US 1998-PV111582 19981209.

AB The present invention provides recombinant vectors encoding and expressing at least three or more costimulatory mols and host cells infected by the vector. The recombinant vector may addnl. contain a gene encoding one or more target antigens or immunol. epitope as well as cytokine, chemokine, or Flt-3L. A **method** of making a recombinant poxvirus, of enhancing an **immune response** of an individual by administering a recombinant vector, and of treating or preventing a disease by activating a T lymphocyte, are also presented. Further describes are a **method** of making a progenitor dendritic cell or dendritic cell, of assesing the efficacy of a vaccine against a target antigen, and of screening for novel immunogenic peptides. The synergistic effect of these costimulatory mols. on the enhanced activation of T cells was demonstrated. The degree of T-cell activation using recombinant vectors contg. genes encoding three costimulatory mols. was far greater than the sum of recombinant vector constructs contg. one costimulatory mol. and greater than the use of two costimulatory mols. Results

employing the triple costimulatory vectors were most dramatic under conditions of either low levels of first signal or low stimulator to T-cell ratios. This phenomenon was obsd. with both isolated CD4+ and CD8+ T cells. The recombinant vectors of the present invention are useful as immunogenes and vaccines against cancer and pathogenic micro-organisms, and in providing host cells, including dendritic cells and splenocytes with enhanced antigen-presenting functions.

L72 ANSWER 8 OF 19 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 2000-558170 [51] WPIDS
CR 2000-303749 [26]
AB WO 200047229 A UPAB: 20001016
NOVELTY - A recombinant polynucleotide (I) comprising a plurality of polynucleotides encoding an identical antigenic peptide, which are operatively linked to each other to enhance their translation and binding of the peptide to major histocompatibility complex (MHC) molecules, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a gene delivery vehicle comprising (I);

(2) a host cell comprising (I);

(3) presenting antigenic epitopes on the surface of an antigen presenting cell comprising introducing (I) so that the antigenic peptide is translated and presented on the surface of the cell;

(4) generating educated immune effector cells comprising culturing (2) with naive immune effector cells so that they proliferate at the expense (2);

(5) an educated immune effector cell, which has been cultured in the presence and at the expense of (2); and

(6) modulating an **immune response** in a subject comprising administering (I), (2), or (5).

ACTIVITY - Immunomodulatory; cytostatic; antibacterial; virucide. No suitable biological data is given.

MECHANISM OF ACTION - Vaccine; gene therapy. No suitable biological data is given.

USE - (I), a host cell comprising (I), or an educated immune effector cell that has been cultured in the presence and at the expense of the host cell are used to modulated an **immune response** in a subject (claimed). (I) is useful in cancer vaccines an in adoptive immunotherapy. (I) can also induce T cell anergy for use in autoimmune disorders. An **immune response** against a pathogen such as a virus or bacteria can also be induced. (I) is also used in assays for predicting the in vivo efficacy of (I), determining the precursor frequency of immune effector cells specific for an antigenic peptide produced by (I), and monitoring the efficacy of (I) once it has been used to modulate an **immune response**.

ADVANTAGE - There is more potent antigen presentation by cells that express multiple copies of an epitope (i.e. that contain (I)) than ones with a single copy. Cells infected with a vector comprising (I) are lyzed more efficiently than cells infected with a virus encoding a single epitope.

Dwg.0/10

L72 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 4
1999:614081 Document No. 131:224456 **Compositions** and **methods** for gene-based vaccines to provoke T cell responses.
Roberts, Bruce L. (Genzyme Corporation, USA). PCT Int. Appl. WO 9947641 A1 19990923, 83 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US6030 19990319. PRIORITY: US 1998-PV78725 19980320.

AB This invention provides a polynucleotide encoding an antigen that is processed and presented with an MHC Class I mol. on an antigen-presenting cell (APC) and an antigen that is processed and presented with an MHC Class II mol. on the APC. It is beneficial to utilize both pathways,

i.e., NHC class I and class II presenting pathways, in the same antigen-presenting cell, to modulate a humoral and a cellular **immune response** in a subject against a given antigen. Nucleotide sequences are also included encoding a peptide motif that promotes retention of the encoded antigen in the endoplasmic reticulum. **Compns**. contg. these polynucleotides are further provided by this invention. **Methods** of increasing presentation of a peptide on the surface of an APC, and APCs produced by the **methods**, are further provided. Also provided are diagnostic and immunomodulatory **methods** using polynucleotides, APCs, and immune effector cells of the invention.

L72 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2001 ACS DUPLICATE 5
1999:613583 Document No. 131:227662 Enhancement of **immune response** to tumor antigens. Kaplan, Johanne; Gregory, Richard J. (Genzyme Corporation, USA). PCT Int. Appl. WO 9946992 A1 19990923, 65 pp. DESIGNATED STATES: W: AU, CA, JP, US; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US6039 19990319. PRIORITY: US 1998-PV78889 19980320.
AB This invention provides **methods** and **compns**. for breaking tolerance to a self-antigen, esp. in the context of a tumor-assocd. antigen. In one embodiment, dendritic cells are transduced to express tumor antigens derived from allogeneic or heterologous species to break immunol. tolerance and induce a cross-reactive **immune response** against the corresponding native or self-antigen.

L72 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2001 ACS
1999:113796 Document No. 130:195740 Membrane-bound cytokine **compositions** and **methods** of modulating an **immune response** using same. Soo, Hoo William (The Immune Response Corporation, USA). PCT Int. Appl. WO 9906544 A1 19990211, 91 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US15622 19980728. PRIORITY: US 1997-902516 19970729.
AB The present invention provides a cellular vaccine having a membrane-bound fusion protein that includes a non-antibody immunomodulatory mol. operatively fused to a heterologous membrane attachment domain. Non-antibody immunomodulatory mols. useful in the invention include immunostimulatory and immunosuppressive mols. such as cytokines. In one embodiment, the invention provides a cellular vaccine having a membrane-bound fusion protein that includes a non-antibody immunomodulatory mol. operatively fused to a heterologous membrane attachment domain and, addnl., a disease-assocd. antigen or immunogenic epitope thereof. Further provided by the invention are **methods** of modulating an **immune response** against a disease-assocd. antigen by administering to an individual a cellular vaccine having a membrane-bound fusion protein that includes a non-antibody immunomodulatory mol. operatively fused to a heterologous membrane attachment domain.

L72 ANSWER 12 OF 19 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
AN 1999-561873 [47] WPIDS
AB WO 9947179 A UPAB: 19991116
NOVELTY - Antigen-presenting cells (APC) are recruited to a predetermined site in a host by administering an APC recruitment or proliferation factor (I) to the site.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:
(1) **method** for enhancing in vivo presentation of an antigen (Ag) into APC by priming a predetermined site with (I) than administering a transgene at the site; and
(2) **method** for identifying (I).
ACTIVITY - Antitumor.
MECHANISM OF ACTION - (I) favor recruitment of APC to a selected site and presentation of the antigen to antigen-presenting cells (APC) induces

a strong **immune response** that destroys tumor cells (cytotoxic T cell response).

USE - Antigen-presenting cells (APC) are used for treatment of cancer when a cancer-specific antigen is subsequently expressed at the site of treatment.

ADVANTAGE - (I) increases transduction of a transgene encoding an antigen into antigen-presenting cells (APC) in vivo, improving site-specific delivery of tumor associated antigens.

Dwg.0/0

L72 ANSWER 13 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS

1999:219700 Document No.: PREV199900219700. Vaccination with a recombinant vaccinia virus encoding a "self" antigen induces autoimmune vitiligo and tumor cell destruction in mice: Requirement for CD4+ T lymphocytes. Overwijk, Willem W.; Lee, David S.; Surman, Deborah R.; Irvine, Kari R.; Touloukian, Christopher E.; Chan, Chi-Chao; Carroll, Miles W.; Moss, Bernard; Rosenberg, Steven A.; Restifo, Nicholas P. (1). (1) National Cancer Institute, Building 10, Room 2B42, Bethesda, MD, 20892-1502 USA. Proceedings of the National Academy of Sciences of the United States of America, (March 16, 1999) Vol. 96, No. 6, pp. 2982-2987. ISSN: 0027-8424. Language: English. Summary Language: English.

AB Many human and mouse tumor antigens are normal, nonmutated tissue differentiation antigens. Consequently, immunization with these "self" antigens could induce autoimmunity. When we tried to induce **immune responses** to five mouse melanocyte differentiation antigens, **gp100**, MART-1, tyrosinase, and tyrosinase-related proteins (**TRP**) **1** and **TRP-2**, we observed striking depigmentation and melanocyte destruction only in the skin of mice inoculated with a vaccinia virus encoding mouse **TRP-1**. These mice rejected a lethal challenge of B16 melanoma, indicating the **immune response** against **TRP-1** could destroy both normal and malignant melanocytes. Cytotoxic T lymphocytes specific for **TRP-1** could not be detected in depigmented mice, but high titers of IgG anti-**TRP-1** antibodies were present. Experiments with knockout mice revealed an absolute dependence on major histocompatibility complex class II, but not major histocompatibility complex class I, for the induction of both vitiligo and tumor protection. Together, these results suggest that the deliberate induction of self-reactivity using a recombinant viral vector can lead to tumor destruction, and that in this model, CD4+ T lymphocytes are an integral part of this process. Vaccine strategies targeting tissue differentiation antigens may be valuable in cancers arising from nonessential cells and organs such as melanocytes, prostate, testis, breast, and ovary.

L72 ANSWER 14 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS

1999:433511 Document No.: PREV199900433511. High level antibody response to retrovirus-associated but not to melanocyte lineage-specific antigens in mice protected against B16 melanoma. Sfondrini, Lucia; Morelli, Daniele; Bodini, Alessandra; Colnaghi, Maria I.; Menard, Sylvie; Balsari, Andrea (1). (1) Molecular Targeting Unit, Department of Experimental Oncology, Istituto Nazionale Tumori, Via Venezian 1, 20133, Milan Italy. International Journal of Cancer, (Sept. 24, 1999) Vol. 83, No. 1, pp. 107-112. ISSN: 0020-7136. Language: English. Summary Language: English.

AB Mice vaccinated with Mycobacterium tuberculosis Ag38 genetransduced B16 melanoma cells showed significant protection from intravenous challenge with parental B16 melanoma cells. No cytotoxic T-cell activity was found against melanoma cells, although the endogenous presence of the mycobacterial gene induced a preferential Th1 response. After immunization, a low serological response against melanoma cells was detected, while a high titer of antibodies directed to parental B16 cells, mainly of IgG2a isotype, was found in protected mice after challenge. These antibodies exhibited complement-dependent cytotoxicity against melanoma cells in vitro, while in vivo, used in passive immunization, they induced a decrease in a number of experimental B16 lung metastases. Most

of the antibodies were directed against endogenous murine leukemia viruses. No reactivity against melanocyte lineage-specific antigens was observed. In particular, no reactivity was found in sera from protected mice againsttyrosinase-related protein 2 (**TRP-2**), either stably expressed in a non-melanoma cell line or obtained by in vitro transcription-translation, or against tyrosinase, **TRP-1** and **gp100** antigens immunoprecipitated from B16 cells. Thus, in the B16 murine model, the presence of dominant viral antigens induces a very strong humoral response that might be protective and may inhibit or mask the presence of minor clonotypes.

L72 ANSWER 15 OF 19 MEDLINE DUPLICATE 6

1998355607 Document Number: 98355607. PubMed ID: 9692858. Generation of polyclonal rabbit antisera to mouse melanoma associated antigens using gene gun immunization. Surman D R; Irvine K R; Shulman E P; Allweis T M; Rosenberg S A; Restifo N P. (Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.) JOURNAL OF IMMUNOLOGICAL METHODS, (1998 May 1) 214 (1-2) 51-62. Journal code: IFE; 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Lymphocytes from patients with melanoma have been used to clone melanoma associated antigens which are, for the most part, nonmutated melanocyte tissue differentiation antigens. To establish a mouse model for the use of these 'self' antigens as targets for anti-tumor **immune responses**, we have employed the mouse homologues of the human melanoma antigens Tyrosinase, **Tyrosinase Related Protein-1** (**TRP-1**), **gp100**, and MART-1. We sought to generate antisera against these proteins for use in the construction of experimental recombinant and synthetic anti-cancer vaccines, and for use in biologic studies. Using genes cloned from the B16 mouse melanoma or from murine melanocytes, we immunized rabbits with plasmid DNAs coated onto microscopic gold beads that were then delivered using a hand-held, helium-driven 'gene gun'. This strategy enabled us to generate polyclonal rabbit sera containing antibodies that specifically recognized each antigen, as measured by immunostaining of vaccinia virus infected cells. The sera that we generated specifically for **TRP-1**, **gp100**, and MART-1 recognized extracts of the spontaneous murine melanoma, B16. The identities of the recognized proteins was confirmed by Western blot analysis. The titers and specificities of these antisera were determined using ELISA. Interestingly, serum samples generated against murine MART-1 and **gp100** developed antibodies that were cross-reactive with the corresponding human homologues. Recognition of human **gp100** and murine Tyrosinase appeared to be dependent upon conformational epitopes since specificity was lost upon denaturation of the antigens. These antisera may be useful in the detection, purification and characterization of the mouse homologues of recently cloned human tumor associated antigens and may enable the establishment of an animal model of the immune consequences of vaccination against 'self antigens.

L72 ANSWER 16 OF 19 BIOSIS COPYRIGHT 2001 BIOSIS

1998:305757 Document No.: PREV199800305757. The immunogenic properties of melanoma-associated antigens recognized by cytotoxic T lymphocytes. Kirkin, Alexei F.; Dzhandzhugazyan, Karine; Zeuthen, Jesper (1). (1) Dep. Tumor Cell Biol., Inst. Cancer Biol., Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen Denmark. Experimental and Clinical Immunogenetics, (April, 1998) Vol. 15, No. 1, pp. 19-32. ISSN: 0254-9670. Language: English.

AB During the last 6 years significant progress has been achieved in the identification of melanoma-associated antigens recognized by cytotoxic T lymphocytes. These antigens belong to three main groups: tumor-associated testis-specific antigens (MAGE, BAGE, GAGE and PRAME), melanocyte differentiation antigens (tyrosinase, Melan-A/MART-1, **gp100**, **TRP-1** and **TRP-2**) and mutated or aberrantly expressed antigens (MUM-1, CDK4, beta-catenin, **gp100** -in4, p15 and N-acetylglucosaminyltransferase V). In this review, we have

summarized the available data concerning the characterization of melanoma-associated antigens with focus on their immunogenic and protective properties. The development of a strong **immune response** against differentiation antigens is limited by the existence of tolerance against these 'self antigens, permitting the involvement of only T cells with low affinity T cell receptors. Among the melanoma differentiation antigens, only **gp100** has been shown to be a tumor regression antigen. The testis-specific antigens such as MAGE and PRAME should potentially be highly immunogenic antigens. They contain several potential HLA class I binding epitopes and are present only in the testes which are not accessible to the cells of the immune system due to the lack of direct contact with the immune cells and the lack of HLA class I expression on the surface of germ cells. But only 2 patients have been found who responded to these antigens in vivo, indicating their genuinely low immunogenicity. A comparison of the predicted secondary structures of these two groups of antigens (testis-specific and differentiation antigens) revealed enrichment of long alpha-helical stretches in the testis-specific antigens. We hypothesize that such highly organized structures could diminish the efficiency of the protein unfolding - a necessary step in the proteolytic cleavage by proteasomes - and, therefore, could be responsible for the low immunogenicity of these proteins. In this case, modifications decreasing the stability of these proteins might be a means to improve the **immune response** against these potentially therapeutically useful antigens.

L72 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2001 ACS

1997:717833 Document No. 128:2900 Heterologous vaccination vector for boosting immunizations. Chamberlain, Ronald S.; Irvine, Kari R.; Rosenberg, Steven A.; Restifo, Nicholas P. (Chamberlain, Ronald S., USA; Irvine, Kari R.; United States Dept. of Health and Human Services; Rosenberg, Steven A.; Restifo, Nicholas P.). PCT Int. Appl. WO 9739771 A1 19971030, 41 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US6632 19970421. PRIORITY: US 1996-15893 19960422.

AB This invention describes the use of heterologous vaccination vectors for eliciting an enhanced **immune response** or antigen-specific **immune response**. These immunotherapy therapy **methods** use a recombinant DNA vector such as vaccinia virus vector, fowlpox virus vector or adenovirus vector, and a gene encoding the specific antigen, esp. tumor assocd. antigen such as **gp100**, MART-1, **TRP-1** or **TRP-2**.

L72 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2001 ACS

1996:382920 Document No. 125:50737 Enhanced **immune response** by introduction of costimulatory molecule gene into recombinant virus expressing antigen of disease-causing agent. Rosenberg, Steven A.; Restifo, Nicholas P.; Moss, Bernard (United States Dept. of Health and Human Services, USA). PCT Int. Appl. WO 9611279 A2 19960418, 136 pp. DESIGNATED STATES: W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US12638 19951002. PRIORITY: US 1994-317402 19941003; US 1995-474639 19950607.

AB The present invention is a recombinant virus which has incorporated into its genome or portion thereof a gene encoding an antigen of a disease-causing agent in combination with an immunostimulatory mol. for the purpose of stimulating an **immune response** against

the disease causing agent. **Methods** of treatment of diseases such as cancer and diseases caused by pathogenic microorganisms are provided using the recombinant virus. Recombinant vaccinia viruses expressing B7.1 antigen and model tumor-assocd. antigen .beta.-galactosidase were prepd. and shown to mediate tumor regression in mice.

L72 ANSWER 19 OF 19 MEDLINE DUPLICATE 7
96293140 Document Number: 96293140. PubMed ID: 8683899. Human melanoma antigens recognized by T lymphocytes. Kawakami Y; Robbins P F; Rosenberg S A. (Surgery Branch, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892-1502, USA.) KEIO JOURNAL OF MEDICINE, (1996 Jun) 45 (2) 100-8. Ref: 78. Journal code: KUJ; 0376354. ISSN: 0022-9717. Pub. country: Japan. Language: English.

AB Human melanoma antigens and their epitopes recognized by T cells have been identified using a variety of **methods**. These antigens are classified as 1) melanocyte specific melanosomal proteins (MART-1, **gp100**, tyrosinase and **TRP-1**), 2) proteins expressed in testis and a variety of cancers (MAGE-1, MAGE-3, BAGE and GAGE), 3) tumor specific mutated proteins (beta-catenin, MUM-1 and CDK4), and 4) others (p15). Some of the HLA-A2 binding non-mutated melanoma epitopes contained non-dominant anchor amino acids and have relatively low HLA-A2 binding affinity, suggesting that these epitopes were likely to be subdominant or cryptic self determinants. The significant correlation observed between vitiligo development and IL2 based immunotherapy suggested that autoreactive T cells specific for these self peptides were involved in melanoma regression in vivo. In addition, since adoptive transfer into patients of CTL recognizing these epitopes resulted in tumor regression, these epitopes may be tumor rejection antigens. Melanoma reactive CTL were efficiently induced from PBL of patients by in vitro stimulation with PBMC pulsed with these melanoma epitopes and may be useful in adoptive transfer protocols for the treatment of patients with metastatic melanoma. An immunization trial using the MART-1 and **gp100** peptides in conjunction with incomplete Freund's adjuvant is in progress. These identified antigens may be useful for the development of new immunotherapies for the treatment of melanoma patients as well as for understanding the mechanisms of anti-tumor **immune responses** and autoimmune disorders against melanocytes.

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DIALOG INFORMATION SERVICES
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### Status: Signing onto Dialog
 ********
ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS? ********
Welcome to DIALOG
### Status: Connected


Dialog level 01.08.22D

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Logon file405 04oct01 08:56:19
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55,349.
* * *
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 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
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 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
?b picks

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>>>         352 is unauthorized
>>>2 of the specified files are not available
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SYSTEM:OS  - DIALOG OneSearch
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         (c) 2001 BIOSIS
  File  55:Biosis Previews(R)  1993-2001/Sep W5
         (c) 2001 BIOSIS
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File 159:Cancerlit 1975-[redacted]01/Aug
(c) format only 2001 Dialog Corporation
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(c) 2001 The HW Wilson Co
File 358:Current BioTech Abs 1983-2001/Aug
(c) 2001 DECHEMA
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File 340:CLAIMS(R)/US PATENT 1950-01/Sep 18
(c) 2001 IFI/CLAIMS(R)
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File 155:MEDLINE(R) 1966-2001/Oct W4
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shortly. Additional coverage added. See HELP NEWS 349.

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S3	0	S2 AND GP75

?t s2/5/all

2/5/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)
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12874594 BIOSIS NO.: 200100081743
Identification and characterization of a spliced C-type lectin-like gene encoded by rat cytomegalovirus.
AUTHOR: Voigt Sebastian; Sandford Gordon R; Ding Lijun; Burns William H(a)
AUTHOR ADDRESS: (a)8701 Watertown Plank Rd., MFRC 6033, Milwaukee, WI, 53226: wburns@mcw.edu**USA
JOURNAL: Journal of Virology 75 (2):p603-611 January, 2001
MEDIUM: print
ISSN: 0022-538X
DOCUMENT TYPE: Article

·RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The English isolate of rat cytomegalovirus (RCMV) encodes a 20-kDa protein with a C-type lectin-like domain that is expressed in the delayed-early and late phases of the viral replication cycle. Genomic sequence analysis of the restriction fragment KpnR of RCMV revealed significant homology to several C-type lectin-containing molecules implicated in natural killer (NK) and T-cell interactions, as well as genes from four poxviruses and African swine fever virus. The gene is spliced into five exons and shows a splicing pattern with exon boundaries similar to those observed in the human differentiation antigen CD69. The cap site of the gene was mapped by RNase protection, 5' rapid amplification of cDNA ends, and primer extension experiments. This analysis demonstrated that the core promoter of the RCMV lectin-like gene contains a GATA rather than a TATA box. Splicing patterns were confirmed with isolates from an infected-cell cDNA library. A unique aspect of the protein is that its translation is not initiated by the canonical methionine but rather by alanine. To study its role in virus replication and pathogenesis, a recombinant virus was constructed in which the gene is interrupted. Replication in tissue culture was similar to that of wild-type virus.

REGISTRY NUMBERS: 56-41-7Q: ALANINE; 302-72-7Q: ALANINE
DESCRIPTORS:
MAJOR CONCEPTS: Molecular Genetics (Biochemistry and Molecular Biophysics); Infection
BIOSYSTEMATIC NAMES: Animal Viruses--Viruses, Microorganisms; Herpesviridae--Animal Viruses, Viruses, Microorganisms; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia; Poxviridae--Animal Viruses, Viruses, Microorganisms
ORGANISMS: African swine fever virus (Animal Viruses)--pathogen; cytomegalovirus (Herpesviridae)--pathogen; poxvirus (Poxviridae)--pathogen; rat (Muridae)--animal model, host
ORGANISMS: PARTS ETC: T cell--blood and lymphatics, immune system; natural killer cells--blood and lymphatics, immune system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animal Viruses; Animals; Chordates; Mammals; Microorganisms; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates; Viruses
CHEMICALS & BIOCHEMICALS: CD-69--*human differentiation antigen*; alanine; lectin
GENE NAME: rat C-type lectin-like gene (Muridae)--mapping
METHODS & EQUIPMENT: RNase protection--gene mapping method; genome sequence analysis--analytical method
MISCELLANEOUS TERMS: viral replication cycle
CONCEPT CODES:
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
02506 Cytology and Cytochemistry-Animal
03502 Genetics and Cytogenetics-General
03506 Genetics and Cytogenetics-Animal
15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
31500 Genetics of Bacteria and Viruses
33506 Virology-Animal Host Viruses
34502 Immunology and Immunochemistry-General; Methods
36006 Medical and Clinical Microbiology-Virology
BIOSYSTEMATIC CODES:
02600 Animal Viruses-General (1993-)
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12 HUMAN MELANOCYTE?
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S4 0 HUMAN MELANOCYTE? AND GP75

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S6          0   S5 AND HUMAN DIFFENTIATION ANTIGEN?
S7       1795   GP100
S8        505   RD (unique items)
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     S14   1030  PSMA
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...examined 50 records  (400)
...examined 50 records  (450)
...examined 50 records  (500)
...examined 50 records  (550)
...examined 50 records  (600)
...examined 50 records  (650)
...examined 50 records  (700)
...examined 50 records  (750)
...examined 50 records  (800)
...examined 50 records  (850)
...examined 50 records  (900)
...examined 50 records  (950)
...examined 50 records  (1000)
...completed examining records
     S15    400  RD (unique items)
?ds

Set     Items   Description
S1          2   HUMAN DIFFERENTIATION ANTIGEN
S2          1   RD (unique items)
S3          0   S2 AND GP75
S4          0   HUMAN MELANOCYTE? AND GP75
S5        671   GP75
```

```
S6          0   S5 AND HUM[redacted] DIFFENTIATION ANTIGEN?
S7       1795   GP100
S8        505   RD (unique items)
S9          0   S8 AND DIFFENTIATION ANTIGEN?
S10       671   GP75
S11        58   TRP-2
S12        27   RD (unique items)
S13         0   HUMAN PROSTATE ANTIGEN
S14      1030   PSMA
S15       400   RD (unique items)
?s insect cell line?
     S16      84  INSECT CELL LINE?
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...completed examining records
     S17      42  RD (unique items)
?s s17 and s8
              42  S17
             505  S8
     S18       0  S17 AND S8
?s s17 and s12
              42  S17
              27  S12
     S19       0  S17 AND S12
?s s17 and s15
              42  S17
             400  S15
     S20       0  S17 AND S15
?s s8 and sf9 cells
             505  S8
               2  SF9 CELLS
     S21       0  S8 AND SF9 CELLS
?s s8 and spodoptera frugiperda
             505  S8
             113  SPODOPTERA FRUGIPERDA
     S22       0  S8 AND SPODOPTERA FRUGIPERDA
?s spodoptera frugiperda
     S23     113  SPODOPTERA FRUGIPERDA
?r
>>>Unrecognizable Command
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...examined 50 records  (100)
...completed examining records
     S24     108  RD (unique items)
?s s24 and gp75
             108  S24
             671  GP75
     S25       0  S24 AND GP75
?s s24 and human differentiation antigen
             108  S24
               2  HUMAN DIFFERENTIATION ANTIGEN
     S26       0  S24 AND HUMAN DIFFERENTIATION ANTIGEN
```

?s human melanocytes and g[redacted]
6 HUMAN MELANOCYTES
671 GP75
S27 0 HUMAN MELANOCYTES AND GP75
?s melanocytes and gp75
28895 MELANOCYTES
671 GP75
S28 211 MELANOCYTES AND GP75
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records (50)
...examined 50 records (100)
...examined 50 records (150)
...examined 50 records (200)
...completed examining records
S29 83 RD (unique items)
?s s29 and insect cell line?
83 S29
84 INSECT CELL LINE?
S30 0 S29 AND INSECT CELL LINE?
?s s29 and sf9
83 S29
15883 SF9
S31 1 S29 AND SF9
?t s31/5/all

31/5/1 (Item 1 from file: 349)
DIALOG(R)File 349:PCT Fulltext
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00435110
STIMULATION OF AN IMMUNE RESPONSE TO DIFFERENTIATION ANTIGEN STIMULATED BY ALTERED ANTIGEN
PROCEDE ET COMPOSITIONS DESTINES A STIMULER UNE REPONSE IMMUNE A L'EGARD D'UN ANTIGENE DE DIFFERENCIATION STIMULE PAR UN ANTIGENE MODIFIE
Patent Applicant/Assignee:
SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH,
HOUGHTON Alan,
NAFTZGER Clarissa,
VIJAYASARADHI Setaluri,
Inventor(s):
HOUGHTON Alan,
NAFTZGER Clarissa,
VIJAYASARADHI Setaluri,
Patent and Priority Information (Country, Number, Date):
Patent: WO 9825574 A2 19980618
Application: WO 97US22669 19971210 (PCT/WO US9722669)
Priority Application: US 9632535 19961210; US 9736419 19970217
Designated States: CA JP US AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
Main International Patent Class: A61K-035/12
International Patent Class: A61K-35:56; A61K-39:00; C12N-05:06; C12N-05:10; C12N-05:18; C12N-05:22; C12N-15:12; C12N-15:06; C12N-15:63; C12N-15:85
Publication Language: English
Fulltext Availability:
Detailed Description
Claims
Fulltext Word Count: 4838

English Abstract
Tolerance of the immune system for self-differentiation antigens can be

overcome and an immune response stimulated by administration of a therapeutic differentiation antigen. The therapeutic differentiation antigen is altered with respect to the target differentiation antigen in the individual being treated (i.e., the differentiation antigen to which an immune response is desired) in one of three ways. First, the therapeutic differentiation antigen may be syngeneic with the target differentiation antigen, provided that therapeutic differentiation antigen is expressed in cells of a species different from the individual being treated. For example, a human differentiation antigen expressed in insect or other non-human host cells can be used to stimulate an immune response to the differentiation antigen in a human subject. Second, the therapeutic differentiation antigen may be a mutant form of a syngeneic differentiation antigen, for example a glycosylation mutant. Third, the therapeutic differentiation antigen may be a differentiation antigen (wild-type or mutant) of the same type from a species different from the individual being treated. For example, a mouse differentiation antigen can be used to stimulate an immune response to the corresponding differentiation antigen in a human subject. Administration of altered antigens in accordance with the invention results in an effective immunity against the original antigen expressed by the cancer in the treated individual.

French Abstract

Il est possible de dejouer la tolerance du systeme immun a l'egard d'antigenes de differenciation autonome et de stimuler une reponse immune par administration d'un antigene de differenciation therapeutique. On a modifie de trois manieres cet antigene de differenciation therapeutique par rapport a l'antigene de differenciation cible, chez l'individu en cours de traitement (a savoir l'antigene de differenciation vis-a-vis duquel une reponse immune est souhaitee). Premierement, l'antigene de differenciation therapeutique peut etre syngenique avec l'antigene de differenciation cible, a condition que l'antigene de differenciation therapeutique soit exprime dans des cellules d'une espece differente de celle appartenant a l'individu en cours de traitement. Par exemple, on peut utiliser un antigene de differenciation humain exprime dans un insecte ou dans tout autre cellule hote non humaine, afin de stimuler, chez l'homme, une reponse immune a l'egard de l'antigene de differenciation. Deuxiemement, l'antigene de differenciation therapeutique peut etre une forme mutante d'un antigene de differenciation syngenique, par exemple un mutant par glycosylation. Troisiemement, l'antigene de differenciation therapeutique peut etre un antigene de differenciation (de type sauvage ou mutant) du meme type mais provenant d'une espece differant de celle de l'individu en cours de traitement. Par exemple, on peut utiliser un antigene de differenciation de souris pour stimuler chez l'homme une reponse immune a l'egard de l'antigene de differenciation correspondant. L'administration d'antigenes modifies selon l'invention permet d'obtenir, chez l'individu traite, une immunite efficace contre l'antigene original exprime par le cancer.

?ds

Set	Items	Description
S1	2	HUMAN DIFFERENTIATION ANTIGEN
S2	1	RD (unique items)
S3	0	S2 AND GP75
S4	0	HUMAN MELANOCYTE? AND GP75
S5	671	GP75
S6	0	S5 AND HUMAN DIFFENTIATION ANTIGEN?
S7	1795	GP100
S8	505	RD (unique items)
S9	0	S8 AND DIFFENTIATION ANTIGEN?
S10	671	GP75
S11	58	TRP-2
S12	27	RD (unique items)
S13	0	HUMAN PROSTATE ANTIGEN
S14	1030	PSMA
S15	400	RD (unique items)
S16	84	INSECT CELL LINE?

```
S17         42   RD (unique items)
S18          0   S17 AND S8
S19          0   S17 AND S12
S20          0   S17 AND S15
S21          0   S8 AND SF9 CELLS
S22          0   S8 AND SPODOPTERA FRUGIPERDA
S23        113   SPODOPTERA FRUGIPERDA
S24        108   RD (unique items)
S25          0   S24 AND GP75
S26          0   S24 AND HUMAN DIFFERENTIATION ANTIGEN
S27          0   HUMAN MELANOCYTES AND GP75
S28        211   MELANOCYTES AND GP75
S29         83   RD (unique items)
S30          0   S29 AND INSECT CELL LINE?
S31          1   S29 AND SF9
?s s24 and gp100
             108  S24
            1795  GP100
     S32       0  S24 AND GP100
?s s24 and trp-2
             108  S24
              58  TRP-2
     S33       0  S24 AND TRP-2
?s s24 and psma
             108  S24
            1030  PSMA
     S34       0  S24 AND PSMA
?s s24 and human prostate antigen
             108  S24
               0  HUMAN PROSTATE ANTIGEN
     S35       0  S24 AND HUMAN PROSTATE ANTIGEN
?ds

Set     Items   Description
S1          2   HUMAN DIFFERENTIATION ANTIGEN
S2          1   RD (unique items)
S3          0   S2 AND GP75
S4          0   HUMAN MELANOCYTE? AND GP75
S5        671   GP75
S6          0   S5 AND HUMAN DIFFENTIATION ANTIGEN?
S7       1795   GP100
S8        505   RD (unique items)
S9          0   S8 AND DIFFENTIATION ANTIGEN?
S10       671   GP75
S11        58   TRP-2
S12        27   RD (unique items)
S13         0   HUMAN PROSTATE ANTIGEN
S14      1030   PSMA
S15       400   RD (unique items)
S16        84   INSECT CELL LINE?
S17        42   RD (unique items)
S18         0   S17 AND S8
S19         0   S17 AND S12
S20         0   S17 AND S15
S21         0   S8 AND SF9 CELLS
S22         0   S8 AND SPODOPTERA FRUGIPERDA
S23       113   SPODOPTERA FRUGIPERDA
S24       108   RD (unique items)
S25         0   S24 AND GP75
S26         0   S24 AND HUMAN DIFFERENTIATION ANTIGEN
S27         0   HUMAN MELANOCYTES AND GP75
S28       211   MELANOCYTES AND GP75
S29        83   RD (unique items)
S30         0   S29 AND INSECT CELL LINE?
S31         1   S29 AND SF9
S32         0   S24 AND GP100
S33         0   S24 AND TRP-2
```

```
S34          0   S24 AND PS
S35          0   S24 AND HUMAN PROSTATE ANTIGEN
?non-human cell line
>>>Unrecognizable Command
?s non-human cell line
     S36       0  NON-HUMAN CELL LINE
?s human diffentiation antigen
     S37       0  HUMAN DIFFENTIATION ANTIGEN
?s differentiation antigen
     S38    1396  DIFFERENTIATION ANTIGEN
?s s38 and human
            1396  S38
        25921534  HUMAN
     S39     997  S38 AND HUMAN
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...examined 50 records  (300)
...examined 50 records  (350)
...examined 50 records  (400)
...examined 50 records  (450)
...examined 50 records  (500)
...examined 50 records  (550)
...examined 50 records  (600)
...examined 50 records  (650)
...examined 50 records  (700)
...examined 50 records  (750)
...examined 50 records  (800)
...examined 50 records  (850)
...examined 50 records  (900)
...examined 50 records  (950)
...completed examining records
     S40     703  RD (unique items)
?ds

Set     Items   Description
S1          2   HUMAN DIFFERENTIATION ANTIGEN
S2          1   RD (unique items)
S3          0   S2 AND GP75
S4          0   HUMAN MELANOCYTE? AND GP75
S5        671   GP75
S6          0   S5 AND HUMAN DIFFENTIATION ANTIGEN?
S7       1795   GP100
S8        505   RD (unique items)
S9          0   S8 AND DIFFENTIATION ANTIGEN?
S10       671   GP75
S11        58   TRP-2
S12        27   RD (unique items)
S13         0   HUMAN PROSTATE ANTIGEN
S14      1030   PSMA
S15       400   RD (unique items)
S16        84   INSECT CELL LINE?
S17        42   RD (unique items)
S18         0   S17 AND S8
S19         0   S17 AND S12
S20         0   S17 AND S15
S21         0   S8 AND SF9 CELLS
```

```
S22          0   S8 AND SPODOPTERA FRUGIPERDA
S23        113   SPODOPTERA FRUGIPERDA
S24        108   RD (unique items)
S25          0   S24 AND GP75
S26          0   S24 AND HUMAN DIFFERENTIATION ANTIGEN
S27          0   HUMAN MELANOCYTES AND GP75
S28        211   MELANOCYTES AND GP75
S29         83   RD (unique items)
S30          0   S29 AND INSECT CELL LINE?
S31          1   S29 AND SF9
S32          0   S24 AND GP100
S33          0   S24 AND TRP-2
S34          0   S24 AND PSMA
S35          0   S24 AND HUMAN PROSTATE ANTIGEN
S36          0   NON-HUMAN CELL LINE
S37          0   HUMAN DIFFENTIATION ANTIGEN
S38       1396   DIFFERENTIATION ANTIGEN
S39        997   S38 AND HUMAN
S40        703   RD (unique items)
?s s40 and gp75
              703  S40
              671  GP75
     S41        2  S40 AND GP75
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
     S42        2  RD (unique items)
?t s42/5/all

 42/5/1     (Item 1 from file: 72)
DIALOG(R)File  72:EMBASE
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10925663     EMBASE No: 1998320900
```

Tumor immunity and autoimmunity induced by immunization with homologous DNA

Weber L.W.; Bowne W.B.; Wolchok J.D.; Srinivasan R.; Qin J.; Moroi Y.; Clynes R.; Song P.; Lewis J.J.; Houghton A.N.
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AUTHOR EMAIL: a-houghton@ski.mskcc.org
Journal of Clinical Investigation (J. CLIN. INVEST.) (United States)
15 SEP 1998, 102/6 (1258-1264)
CODEN: JCINA ISSN: 0021-9738
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 37

The immune system can recognize self antigens expressed by cancer cells. Differentiation antigens are prototypes of these self antigens, being expressed by cancer cells and their normal cell counterparts. The tyrosinase family proteins are well characterized differentiation antigens recognized by antibodies and T cells of patients with melanoma. However, immune tolerance may prevent immunity directed against these antigens. Immunity to the brown locus protein, *gp75*/tyrosinase-related protein-1, was investigated in a syngeneic mouse model. C57BL/6 mice, which are tolerant to *gp75*, generated autoantibodies against *gp75* after immunization with DNA encoding *human* *gp75* but not syngeneic mouse *gp75*. Priming with *human* *gp75* DNA broke tolerance to mouse *gp75*. Immunity against mouse *gp75* provided significant tumor protection. Manifestations of autoimmunity were observed, characterized by coat

depigmentation. Rejection of tumor challenge required CD4sup + and NK1.1sup + cells and Fc receptor gamma-chain, but depigmentation did not require these components. Thus, immunization with homologous DNA broke tolerance against mouse *gp75*, possibly by providing help from CD4sup + T cells. Mechanisms required for tumor protection were not necessary for autoimmunity, demonstrating that tumor immunity can be uncoupled from autoimmune manifestations.

DRUG DESCRIPTORS:
*dna
differentiation antigen; monophenol monooxygenase; glycoprotein; autoantibody--endogenous compound--ec; cd4 antigen--endogenous compound--ec ; Fc receptor--endogenous compound--ec
MEDICAL DESCRIPTORS:
*tumor immunity; *autoimmunity; *immunization
antigen recognition; immunological tolerance; melanoma; protein family; depigmentation; tumor rejection; nonhuman; female; mouse; animal experiment ; animal model; controlled study; animal tissue; animal cell; article; priority journal
CAS REGISTRY NO.: 9007-49-2 (DNA); 9002-10-2 (monophenol monooxygenase)
SECTION HEADINGS:
013 Dermatology and Venereology
016 Cancer
022 *Human* Genetics
026 Immunology, Serology and Transplantation

42/5/2 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

07364033 EMBASE No: 1998271225
Adenovirus-mediated expression of melanoma antigen *gp75* as immunotherapy for metastatic melanoma
Hirschowitz E.A.; Leonard S.; Song W.; Ferris B.; Leopold P.L.; Lewis J.J.; Bowne W.B.; Wang S.; Houghton A.N.; Crystal R.G.
R.G. Crystal, Div Pulmonary Critical Care Medicine, The New York Hospital, Cornell Medical Center, 520 East 70th Street, New York, NY 10021 United States
Gene Therapy (GENE THER.) (United Kingdom) 1998, 5/7 (975-983)
CODEN: GETHE ISSN: 0969-7128
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 83

Melanocyte differentiation antigens, such as the brown locus protein *gp75*, are potential biological targets for immunotherapy. We investigated whether expression of the murine *gp75* cDNA mediated by an adenovirus (Ad) vector could induce melanoma rejection using this model self antigen that usually induces tolerance, and whether Ad vector-directed production of interleukin-2 (IL2) might augment this response. To evaluate this approach, Ad vectors were constructed containing the murine *gp75* cDNA (Ad.*gp75*) and the *human* IL2 cDNA (Ad.IL2). Efficacy was evaluated in C57Bl/6 mice challenged i.v. with 10sup 5 B16 cells, using the number of lung metastases as the efficacy parameter. Naive control mice developed 175 +/- 12 metastases by day 14. Controls receiving intranasal Ad.IL2 1 day after B16 cell injection, intraperitoneal (i.p.) mitomycin-C-treated B16 cells +/- i.p. Ad.IL2 before B16 cell challenge and Ad.betagal-treated mice had similar numbers of metastases as controls ($P > 0.1$). In marked contrast, preimmunization with intradermal Ad.*gp75* provided dramatic reduction in the number of lung metastases (52 +/- 7, 29% of control). Addition of regional (intranasal delivery to the lung) Ad.IL2 to intradermal Ad.*gp75* preiminunization 1 day following tumor challenge provided further protection (18 +/- 6, 10% of control). Depletion of CD4sup + and CD8sup + T-cell subsets effectively blocked the protective effect seen following immunization. Adoptive transfer of macrophage-depleted splenocytes from Ad. *gp75*-immunized mice similarly afforded significant protection against B16

tumor cell challenge. Furthermore, serum obtained 21 days following Ad.*gp75* immunization showed no detectable anti-*gp75* antibody by immunoprecipitation. These results suggest that immunization with Ad.*gp75* induces cellular immune responses that are capable of rejecting B16 melanoma in a host that is usually tolerant to *gp75* antigen.

DRUG DESCRIPTORS:
*melanoma antigen
differentiation antigen; complementary dna; protein; interleukin 2; cd4 antigen--endogenous compound--ec; dna vaccine
MEDICAL DESCRIPTORS:
*adenovirus; *immunotherapy; *melanoma--therapy--th
melanocyte; virus expression; expression vector; tumor cell; t lymphocyte; lung metastasis; adoptive transfer; cellular immunity; melanoma b16 --therapy--th; nonhuman; mouse; animal experiment; animal model; controlled study; animal tissue; animal cell; article; priority journal
CAS REGISTRY NO.: 67254-75-5 (protein); 85898-30-2 (interleukin 2)
SECTION HEADINGS:
  004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
  016 Cancer
  022 *Human* Genetics
  026 Immunology, Serology and Transplantation
  029 Clinical and Experimental Biochemistry
?ds

Set	Items	Description
S1	2	HUMAN DIFFERENTIATION ANTIGEN
S2	1	RD (unique items)
S3	0	S2 AND GP75
S4	0	HUMAN MELANOCYTE? AND GP75
S5	671	GP75
S6	0	S5 AND HUMAN DIFFENTIATION ANTIGEN?
S7	1795	GP100
S8	505	RD (unique items)
S9	0	S8 AND DIFFENTIATION ANTIGEN?
S10	671	GP75
S11	58	TRP-2
S12	27	RD (unique items)
S13	0	HUMAN PROSTATE ANTIGEN
S14	1030	PSMA
S15	400	RD (unique items)
S16	84	INSECT CELL LINE?
S17	42	RD (unique items)
S18	0	S17 AND S8
S19	0	S17 AND S12
S20	0	S17 AND S15
S21	0	S8 AND SF9 CELLS
S22	0	S8 AND SPODOPTERA FRUGIPERDA
S23	113	SPODOPTERA FRUGIPERDA
S24	108	RD (unique items)
S25	0	S24 AND GP75
S26	0	S24 AND HUMAN DIFFERENTIATION ANTIGEN
S27	0	HUMAN MELANOCYTES AND GP75
S28	211	MELANOCYTES AND GP75
S29	83	RD (unique items)
S30	0	S29 AND INSECT CELL LINE?
S31	1	S29 AND SF9
S32	0	S24 AND GP100
S33	0	S24 AND TRP-2
S34	0	S24 AND PSMA
S35	0	S24 AND HUMAN PROSTATE ANTIGEN
S36	0	NON-HUMAN CELL LINE
S37	0	HUMAN DIFFENTIATION ANTIGEN
S38	1396	DIFFERENTIATION ANTIGEN
S39	997	S38 AND HUMAN
S40	703	RD (unique items)
S41	2	S40 AND GP75

S42 2 RD (unique items)
?s s40 and gp100
703 S40
1795 GP100
S43 9 S40 AND GP100
?rd
>>>Duplicate detection is not supported for File 340.
>>>Duplicate detection is not supported for File 344.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 447.
>>>Duplicate detection is not supported for File 349.

>>>Records from unsupported files will be retained in the RD set.
...completed examining records
S44 9 RD (unique items)
?t s44/5/all

44/5/1 (Item 1 from file: 5)

12872616 BIOSIS NO.: 200100079765
Intracutaneous genetic immunization with autologous melanoma-associated antigen Pmel17/*gp100* induces T cell-mediated tumor protection in vivo.
AUTHOR: Wagner Stephan N(a); Wagner Christine; Luehrs Petra; Weimann Tatjana K; Kutil Raphaela; Goos Manfred; Stingl Georg; Schneeberger Achim
AUTHOR ADDRESS: (a)Klinik und Poliklinik fuer Dermatologie, Venerologie und Allergologie, Universitaetsklinikum Essen, Hufelandstr. 55, D-45122, Essen: stephan.wagner@uni-essen.de**Germany
JOURNAL: Journal of Investigative Dermatology 115 (6):p1082-1087 December, 2000
MEDIUM: print
ISSN: 0022-202X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Using the differentiation antigen Pmel17/*gp100* to genetically immunize C57BL/6 mice (H-2b), we and others noticed that only mice that had received the *human* homolog but not animals injected with the murine counterpart were protected against the growth of syngeneic B16 melanoma cells. The goal of this study was to determine whether the state of non-responsiveness to the autoantigen Pmel17/*gp100* can be broken by immunization with a plasmid DNA construct encoding the autologous form of the molecule. A construct containing the murine form of Pmel17 was administered intradermally to DBA/2 mice (H-2d), which were then investigated for the presence of Pmel17/*gp100*-specific immunity. We show that administration of plasmid DNA coding for the autologous melanoma-associated antigen Pmel17/*gp100* protects DBA/2 mice against the growth of Pmel17-positive M3 melanoma cells but not against Pmel17-negative M3 melanoma cells or unrelated P815 mastocytoma cells. Cell depletion experiments demonstrated that this protective effect is mediated by T lymphocytes. The notion that Pmel17/*gp100* represents the biologically relevant target in this system was supported by the observations (i) that recipients of Pmel17/*gp100* DNA mount an antigen-specific cytotoxic T lymphocyte response and (ii) that M3 tumors growing in mice immunized with autologous Pmel17/*gp100* had lost expression of this melanoma-associated antigen whereas M3 melanomas appearing in control-vector-treated animals were still Pmel17/*gp100* -positive. These results indicate that intracutaneous genetic immunization with autologous melanoma-associated antigen Pmel17/*gp100* encoding plasmid DNA can lead to protection against melanoma cells as a result of the induction of a melanoma-associated antigen-specific and protective T-cell-mediated immune response.

DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Integumentary System (Chemical Coordination and Homeostasis); Tumor Biology
BIOSYSTEMATIC NAMES: Animalia; Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: B16 cell line (Muridae)--murine melanoma cells; M3 cell line (Animalia)--animal melanoma cells; P815 cell line (Muridae)--murine mastocytoma cells; mouse (Muridae)--animal model
ORGANISMS: PARTS ETC: T cells--blood and lymphatics, immune system; T lymphocytes--blood and lymphatics, immune system
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Mammals; Nonhuman Mammals; Nonhuman Vertebrates; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: Pmel17/*gp100*--*differentiation antigen*
METHODS & EQUIPMENT: genetic immunization--immunization method, intracutaneous administration, therapeutic method
MISCELLANEOUS TERMS: immune response; tumor growth; tumor protection
CONCEPT CODES:
34502 Immunology and Immunochemistry-General; Methods
02506 Cytology and Cytochemistry-Animal
10060 Biochemical Studies-General
12512 Pathology, General and Miscellaneous-Therapy (1971-)
15002 Blood, Blood-Forming Organs and Body Fluids-Blood and Lymph Studies
15004 Blood, Blood-Forming Organs and Body Fluids-Blood Cell Studies
18504 Integumentary System-Physiology and Biochemistry
24003 Neoplasms and Neoplastic Agents-Immunology
24004 Neoplasms and Neoplastic Agents-Pathology; Clinical Aspects; Systemic Effects
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology

44/5/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11054820 BIOSIS NO.: 199799675965
Melanoma associated antigen expression in advanced primary cutaneous melanoma.
AUTHOR: Heisele O; Ancans J; Engele L
AUTHOR ADDRESS: Lab. Biomodulators, BMC, Riga**Latvia
JOURNAL: Melanoma Research 7 (SUPPL. 1):pS139 1997
CONFERENCE/MEETING: 4th World Conference on Melanoma Sydney, Australia June 10-14, 1997
ISSN: 0960-8931
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 9002-10-2: TYROSINASE
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Clinical Immunology (*Human* Medicine, Medical Sciences); Dermatology (*Human* Medicine, Medical Sciences); Development; Integumentary System (Chemical Coordination and Homeostasis); Mathematical Biology (Computational Biology); Metabolism; Oncology (*Human* Medicine, Medical Sciences); Pathology; Pharmacology; Public Health (Allied Medical Sciences); Surgery (Medical Sciences
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: *human* (Hominidae)
BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): animals; chordates; humans; mammals; primates; vertebrates
CHEMICALS & BIOCHEMICALS: TYROSINASE
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Poster; ADVANCED PRIMARY CUTANEOUS MELANOMA; CLINICAL IMMUNOLOGY; DERMATOLOGY; *DIFFERENTIATION ANTIGEN*; EXPRESSION; GLYCOPROTEIN 100; *GP100*; IMMUNOLOGIC METHOD; IMMUNOTHERAPY; INTEGUMENTARY SYSTEM DISEASE; MAGE-1; MAGE-3; MART-1; MELANOMA ASSOCIATED ANTIGEN; NEOPLASTIC DISEASE; ONCOLOGY; PATIENT; PROGRESSION ANTIGEN; STATISTICAL ANALYSIS; SURGERY; SURGICAL METHOD; THERAPEUTIC METHOD; TUMOR THICKNESS; TUMOR VACCINE; TYROSINASE

CONCEPT CODES:
04500 Mathematical Biology and Statistical Methods
10064 Biochemical Studies-Proteins, Peptides and Amino Acids
11105 Anatomy and Histology, General and Comparative-Surgery
12512 Pathology, General and Miscellaneous-Therapy (1971-)
13012 Metabolism-Proteins, Peptides and Amino Acids
18504 Integumentary System-Physiology and Biochemistry
18506 Integumentary System-Pathology
22005 Pharmacology-Clinical Pharmacology (1972-)
22018 Pharmacology-Immunological Processes and Allergy
22020 Pharmacology-Integumentary System, Dental and Oral Biology
24003 Neoplasms and Neoplastic Agents-Immunology
24006 Neoplasms and Neoplastic Agents-Biochemistry
24008 Neoplasms and Neoplastic Agents-Therapeutic Agents; Therapy
25508 Developmental Biology-Embryology-Morphogenesis, General
34508 Immunology and Immunochemistry-Immunopathology, Tissue Immunology
37010 Public Health-Public Health Administration and Statistics
37012 Public Health-Health Services and Medical Care
00520 General Biology-Symposia, Transactions and Proceedings of Conferences, Congresses, Review Annuals
BIOSYSTEMATIC CODES:
86215 Hominidae

44/5/3 (Item 1 from file: 72)
DIALOG(R)File 72:EMBASE

07808498 EMBASE No: 1999297966
Establishment of *gp100* and MART-1/Melan-A-specific cytotoxic T lymphocyte clones using in vitro immunization against preselected highly immunogenic melanoma cell clones
Kirkin A.F.; Straten P.T.; Hansen M.R.; Barfoed A.; Dzhandzhugazyan K.N.; Zeuthen J.
A.F. Kirkin, Department of Tumour Cell Biology, Institute of Cancer Biology, Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen Denmark
AUTHOR EMAIL: jz@bio.cancer.dk
Cancer Immunology Immunotherapy (CANCER IMMUNOL. IMMUNOTHER.) (Germany)
1999, 48/5 (239-246)
CODEN: CIIMD ISSN: 0340-7004
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 29

The induction of an in vitro T cell response against tumour-associated antigens with subsequent expansion of the individual cytotoxic T lymphocyte (CTL) clones still is not routine and the only tumour-associated antigen that has been found to easily induce the establishment of CTL clones is the MART- 1/Melan-A antigen. In this paper, we describe a new approach for in vitro immunization based on the use of preselected melanoma cell clones. The *human* melanoma cell subline FM3.P was cloned and the immunological properties of individual clones were compared. Melanoma cell clone FM3.29, having a high level of expression of melanoma differentiation antigens, as well as high levels of the HLA class I and class II antigens and adhesion molecules, was used for the establishment of a CTL line that was subsequently cloned. For optimization of the conditions of growth of established CTL clones, a particular melanoma subline FM3.D/40 was selected for supporting the proliferation of CTL clones. The majority of the established CTL clones recognized the melanoma-associated differentiation antigens *gp100* and MART- 1/Melan-A. Epitope analysis indicated that two different epitopes derived from *gp100* (154-162 and 280-288) and a single epitope from MART-1/Melan-A (27-35) were recognized by these CTL clones. The *gp100*-specific CTL clones were found to be significantly more sensitive to the culture conditions than the MART-1/Melan-A-specific CTL clones. In addition, the presence of excess peptide in the culture medium induced autokilling of the *gp100*-specific, but not the

MART-1/Melan-A-specific CTL clones. Taken together, these results demonstrate that, by careful preselection of melanoma cell lines and clones both for the induction of CTL line from patients' peripheral blood lymphocytes and subsequent cloning, it is possible to obtain a large number of stable CTL clones even against such an inherently 'difficult' differentiation antigen as *gp100*.

DRUG DESCRIPTORS:
*tumor antigen--endogenous compound--ec; **differentiation antigen* --endogenous compound--ec
HLA antigen class 1--endogenous compound--ec; HLA antigen class 2 --endogenous compound--ec; monophenol monooxygenase--endogenous compound --ec
MEDICAL DESCRIPTORS:
*cancer immunotherapy; *lymphocyte clone
cytotoxic t lymphocyte; immunogenicity; melanoma cell; antigen expression; cell adhesion; mixed lymphocyte culture; *human*; *human cell*; article; priority journal
DRUG TERMS (UNCONTROLLED): glycoprotein gp 100--endogenous compound--ec; melan a antigen--endogenous compound--ec; mart 1 antigen--endogenous compound--ec
CAS REGISTRY NO.: 9002-10-2 (monophenol monooxygenase)
SECTION HEADINGS:
026 Immunology, Serology and Transplantation

44/5/4 (Item 2 from file: 72)
DIALOG(R)File 72:EMBASE

07632121 EMBASE No: 1999114502
Vaccination with a recombinant vaccinia virus encoding a 'self' antigen induces autoimmune vitiligo and tumor cell destruction in mice: Requirement for CD4sup + T lymphocytes
Overwijk W.W.; Lee D.S.; Surman D.R.; Irvine K.R.; Touloukian C.E.; Chan C.- C.; Carroll M.W.; Moss B.; Rosenberg S.A.; Restifo N.P.
N.P. Restifo, National Cancer Institute, Building 10, Bethesda, MD 20892-1502 United States
AUTHOR EMAIL: restifo@nih.gov
Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 1999, 96/6 (2982-2987)
CODEN: PNASA ISSN: 0027-8424
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 48

Many *human* and mouse tumor antigens are normal, nonmutated tissue differentiation antigens. Consequently, immunization with these 'self' antigens could induce autoimmunity. When we tried to induce immune responses to five mouse melanocyte differentiation antigens, *gp100*, MART-1, tyrosinase, and tyrosinase-related proteins (TRP) 1 and TRP-2, we observed striking depigmentation and melanocyte destruction only in the skin of mice inoculated with a vaccinia virus encoding mouse TRP-1. These mice rejected a lethal challenge of B16 melanoma, indicating the immune response against TRP-1 could destroy both normal and malignant melanocytes. Cytotoxic T lymphocytes specific for TRP-1 could not be detected in depigmented mice, but high titers of IgG anti-TRP-1 antibodies were present. Experiments with knockout mice revealed an absolute dependence on major histocompatibility complex class II, but not major histocompatibility complex class I, for the induction of both vitiligo and tumor protection. Together, these results suggest that the deliberate induction of self-reactivity using a recombinant viral vector can lead to tumor destruction, and that in this model, CD4sup + T lymphocytes are an integral part of this process. Vaccine strategies targeting tissue differentiation antigens may be valuable in cancers arising from nonessential cells and organs such as melanocytes, prostate, testis, breast, and ovary.

DRUG DESCRIPTORS:
*vaccinia vaccine; *virus vaccine
differentiation antigen--endogenous compound--ec; monophenol monooxygenase--endogenous compound--ec
MEDICAL DESCRIPTORS:
*vaccination; *vitiligo--etiology--et; *tumor cell destruction; *autoimmune disease--etiology--et
helper cell; vaccinia virus; virus recombinant; antibody titer; histocompatibility complex; cancer prevention; antineoplastic activity; tissue distribution; tissue differentiation; melanocyte; nonhuman; female; mouse; animal model; conference paper; priority journal
CAS REGISTRY NO.: 9002-10-2 (monophenol monooxygenase)
SECTION HEADINGS:
026 Immunology, Serology and Transplantation
037 Drug Literature Index

44/5/5 (Item 3 from file: 72)
DIALOG(R)File 72:EMBASE

07400847 EMBASE No: 1998312763
Numbers and differentiation status of melanocytes in idiopathic guttate hypomelanosis
Wallace M.L.; Grichnik J.M.; Prieto V.G.; Shea C.R.
Dr. C.R. Shea, Department of Pathology, Duke University Medical Center, Box 3712, Durham, NC 27710 United States
AUTHOR EMAIL: shea0002@mc.duke.edu
Journal of Cutaneous Pathology (J. CUTANEOUS PATHOL.) (Denmark) 1998, 25/7 (375-379)
CODEN: JCUPB ISSN: 0303-6987
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 31

The etiology and pathogenesis of idiopathic guttate hypomelanosis (IGH) are largely unknown. To investigate whether the pathologic alteration in IGH involves changes in melanocytic differentiation, cell number, or both, we studied nine lesions of IGH by immunoperoxidase, using monoclonal antibodies against the KIT receptor and a panel of melanocyte differentiation antigens (tyrosinase-related protein-1, tyrosinase, and *gp100*/pmel17). In each case, compared with grossly normal non-lesional skin, IGH lesions showed markedly reduced numbers both of KIT+ cells and of cells expressing melanocyte differentiation antigens ($p < 0.0001$). Double immunofluorescence labeling of lesions revealed only scattered cells with a less-differentiated phenotype, i.e. cells positive for KIT but having low or undetectable TRP-1. These results indicate that the pathogenesis of IGH involves an absolute decrease in the number of melanocytes; a block in melanocyte differentiation does not appear to be a major component of the process.

DRUG DESCRIPTORS:
monoclonal antibody; *differentiation antigen*; monophenol monooxygenase; receptor
MEDICAL DESCRIPTORS:
*melanocyte; *hypomelanosis--etiology--et
idiopathic disease; cell count; cell differentiation; immunoperoxidase staining; comparative study; immunofluorescence test; *human*; clinical article; controlled study; *human* tissue; article
CAS REGISTRY NO.: 9002-10-2 (monophenol monooxygenase)
SECTION HEADINGS:
005 General Pathology and Pathological Anatomy
013 Dermatology and Venereology

44/5/6 (Item 4 from file: 72)

07295168 EMBASE No: 1998156423

A103: An anti-Melan-A monoclonal antibody for the detection of malignant melanoma in paraffin-embedded tissues

Jungbluth A.A.; Busam K.J.; Gerald W.L.; Stockert E.; Coplan K.A.; Iversen K.; MacGregor D.P.; Old L.J.; Chen Y.-T.
Dr. A.A. Jungbluth, Ludwig Institute for Cancer Research, Memorial Sloan-Kettering Cancer Ctr., Box 32, 1275 York Avenue, New York, NY 10021 United States

American Journal of Surgical Pathology (AM. J. SURG. PATHOL.) (United States) 1998, 22/5 (595-602)
CODEN: AJSPD ISSN: 0147-5185
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 35

Melan-A is a previously defined, melanocyte differentiation antigen, and an anti-Melan-A murine monoclonal antibody, A103, was recently developed by our group. In this study, we evaluated A103 immunoreactivity on formalin-fixed, paraffin-embedded tissues, exploring the potential of A103 in the diagnosis of metastatic melanoma. Seventy-five metastatic melanomas, 10 primary melanomas, and 10 benign melanocytic nevi were tested. The reactivity of A103 was compared with HMB-4, an anti-*gp100* antibody. Results showed that all nevi were A103 positive, and most primary melanomas were A103 and HMB45 positive. Of 75 metastatic melanomas, 61 (81%) were A103 positive, and 56 (75%) were HMB45 positive. Of 19 HMB45-negative lesions, 8 were A103 positive; of 14 A103-negative lesions, 3 were HMB45 positive. Eleven metastatic lesions, as well as 2 of 10 primary melanomas, were dual negative. These negative cases consisted mainly of the spindle cell and desmoplastic variants. Of the positive cases, A103 showed homogeneous staining in a significantly higher proportion of cases than HMB45 (72% versus 52%). In addition, focal staining with less than 5% reactive tumor cells was seen more frequently in HMB45 (12 of 56) than in A103 (5 of 61). These results indicated that A103 can be used as a first-line antibody in the diagnosis of metastatic melanoma. Our results also showed that A103 reacted with angiomyolipoma, which is known to be HMB45 positive. Of normal tissues, unexpected A 103 reactivity was observed in the adrenal cortex, granulosa and theca cells of the ovary, and Leydig cells of the testis. This A103 immunoreactivity in benign and neoplastic tissues of nonmelanocytic origin, the basis of which is unclear, could also be of potential diagnostic value.

DRUG DESCRIPTORS:
*monoclonal antibody; **differentiation antigen*--endogenous compound--ec; *paraffin
formaldehyde; monoclonal antibody hmb 45; unclassified drug
MEDICAL DESCRIPTORS:
*melanoma--diagnosis--di; *embedding; *cancer diagnosis
melanocyte; tumor differentiation; spindle cell; metastasis--complication --co; metastasis--diagnosis--di; angiomyolipoma--diagnosis--di; melanocytic nevus--diagnosis--di; adrenal cortex; granulosa cell; theca cell; leydig cell; diagnostic value; immunohistochemistry; *human*; major clinical study ; controlled study; *human* tissue; *human* cell; article
DRUG TERMS (UNCONTROLLED): monoclonal antibody a103
CAS REGISTRY NO.: 50-00-0 (formaldehyde)
SECTION HEADINGS:
013 Dermatology and Venereology
016 Cancer
026 Immunology, Serology and Transplantation
037 Drug Literature Index

44/5/7 (Item 5 from file: 72)

07249795 EMBASE No: 1998144592

The immunogenic properties of melanoma-associated antigens recognized by cytotoxic T lymphocytes

Kirkin A.F.; Dzhandzhugazyan K.; Zeuthen J.
Prof. J. Zeuthen, Department of Tumor Cell Biology, Institute of Cancer Biology, Danish Cancer Society, Strandboulevarden 49, DK-2100 Copenhagen Denmark
AUTHOR EMAIL: jz@bio.cancer.dk

Experimental and Clinical Immunogenetics (EXP. CLIN. IMMUNOGENET.) (Switzerland) 1998, 15/1 (19-32)
CODEN: ECIME ISSN: 0254-9670
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 73

During the last 6 years significant progress has been achieved in the identification of melanoma-associated antigens recognized by cytotoxic T lymphocytes. These antigens belong to three main groups: tumor-associated testis-specific antigens (MAGE, BAGE, GAGE and PRAME), melanocyte differentiation antigens (tyrosinase, Melan-A/MART-1, *gp100*, TRP-1 and TRP-2) and mutated or aberrantly expressed antigens (MUM-1, CDK4, beta-catenin, *gp100*-in4, p15 and N-acetylglucosaminyltransferase V). In this review, we have summarized the available data concerning the characterization of melanoma-associated antigens with focus on their immunogenic and protective properties. The development of a strong immune response against differentiation antigens is limited by the existence of tolerance against these 'self' antigens, permitting the involvement of only T cells with low affinity T cell receptors. Among the melanoma differentiation antigens, only *gp100* has been shown to be a tumor regression antigen. The testis-specific antigens such as MAGE and FRAME should potentially be highly immunogenic antigens. They contain several potential HLA class I binding epitopes and are present only in the testes which are not accessible to the cells of the immune system due to the lack of direct contact with the immune cells and the lack of HLA class I expression on the surface of germ cells. But only 2 patients have been found who responded to these antigens in vivo, indicating their genuinely low immunogenicity. A comparison of the predicted secondary structures of these two groups of antigens (testis-specific and differentiation antigens) revealed enrichment of long alpha-helical stretches in the testis-specific antigens. We hypothesize that such highly organized structures could diminish the efficiency of the protein unfolding - a necessary step in the proteolytic cleavage by proteasomes - and, therefore, could be responsible for the low immunogenicity of these proteins. In this case, modifications decreasing the stability of these proteins might be a means to improve the immune response against these potentially therapeutically useful antigens.

DRUG DESCRIPTORS:
*tumor antigen--endogenous compound--ec
t lymphocyte receptor--endogenous compound--ec; *differentiation antigen* --endogenous compound--ec; HLA antigen class 1--endogenous compound--ec; proteasome--endogenous compound--ec
MEDICAL DESCRIPTORS:
*immunogenicity; *antigen recognition; *cytotoxic t lymphocyte antigen expression; immune response; immunological tolerance; testis; germ cell; protein structure; *human*; *human cell*; review; priority journal
SECTION HEADINGS:
013 Dermatology and Venereology
022 *Human* Genetics
026 Immunology, Serology and Transplantation

44/5/8 (Item 6 from file: 72)

06518509 EMBASE No: 1996166125

Inverse relationship of m[redacted]nocyte differentiation antigen [redacted]pression in melanoma tissues and CD8sup + cytotoxic-T-cell responses: Evidence for immunoselection of antigen-loss variants in vivo

Jager E.; Ringhoffer M.; Karbach J.; Arand M.; Ooesch F.; Knuth A.
II. Medizinische Klinik, Hamatologie-Onkologie, Krankenhaus Nordwest, Steinbacher Hohl 2-26,D-60488 Frankfurt Germany
International Journal of Cancer (INT. J. CANCER) (United States) 1996, 66/4 (470-476)
CODEN: IJCNA ISSN: 0020-7136
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Antigenic peptides derived from differentiation antigens of the melanocyte lineage were recently identified in *human* melanomas as targets for MHC-restricted cytotoxic T lymphocytes (CTL). CTL directed against peptides derived from the Melan A/MART-1, tyrosinase and *gp100*/Pmel17 antigens can be detected in melanoma patients and in healthy controls. The presence of defined antigenic peptides and corresponding precursor CTL in patients with metastatic melanoma opens perspectives for the development of antigen-specific tumor vaccines. In this study, we examined the expression of Melan A/MART-1, tyrosinase and *gp100*/Pmel17 in fresh melanoma tissues of HLA-A2sup + patients and the spontaneous CTL reactivity against antigenic peptides derived from these antigens. Our results demonstrate an inverse correlation of antigen expression and CTL response to Melan A/MART-1 and tyrosinase in patients with metastatic melanoma. In 2 patients with advanced disease, CTL responses against Melan A/MART-1 and tyrosinase were induced by intradermal immunization with synthetic nona- or deca-peptides derived from these antigens. Metastases increasing in size over time showed a loss of Melan A/MART-1 expression in the presence of CTL in one patient. The regression of a metastasis with persistent tyrosinase expression was observed in the other patient after the induction of CTL, reactive against tyrosinase. We conclude that CTL responses against melanocyte differentiation antigens may mediate regression of antigen-positive tumors and select for antigen-loss variants in vivo.

DRUG DESCRIPTORS:
*cd8 antigen--endogenous compound--ec; **differentiation antigen* --endogenous compound--ec; *monophenol monooxygenase
unclassified drug
MEDICAL DESCRIPTORS:
*melanocyte; *melanoma
antigen expression; article; controlled study; cytotoxic t lymphocyte; *human*; *human cell*; priority journal; tumor regression
DRUG TERMS (UNCONTROLLED): peptide antigen--endogenous compound--ec
CAS REGISTRY NO.: 9002-10-2 (monophenol monooxygenase)
SECTION HEADINGS:
013 Dermatology and Venereology
016 Cancer
026 Immunology, Serology and Transplantation

44/5/9 (Item 7 from file: 72)
DIALOG(R)File 72:EMBASE

05660081 EMBASE No: 1994074104
Melanocyte lineage-specific antigen *gp100* is recognized by melanoma-derived tumor-infiltrating lymphocytes

Bakker A.B.H.; Schreurs M.W.J.; De Boer A.J.; Kawakami Y.; Rosenberg S.A.; Adema G.J.; Figdor C.G.
Department of Tumor Immunology, Univ. Hospital Nijmegan St. Radboud, Philips van Leydenlaan 25,6525 EX Nijmegen Netherlands
Journal of Experimental Medicine (J. EXP. MED.) (United States) 1994, 179/3 (1005-1009)
CODEN: JEMEA ISSN: 0022-1007
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

We recently isolated a cDNA clone that encodes the melanocyte lineage-specific antigen glycoprotein (gp)100. Antibodies directed against *gp100* are an important tool in the diagnosis of *human* melanoma. Since the *gp100* antigen is highly expressed in melanocytic cells, we investigated whether this antigen might serve as a target for antimelanoma cytotoxic T lymphocytes (CTL). Here, we demonstrate that cytotoxic tumor-infiltrating lymphocytes (TIL) derived from a melanoma patient (TIL 1200) are directed against *gp100*. HLA-A2.1sup + melanoma cells are lysed by TIL from this patient. In addition, murine double transfectants, expressing both HLA-A2.1 and *gp100*, are lysed by TIL 1200, whereas transfectants expressing only HLA-A2.1 are not susceptible to lysis. Furthermore, the HLA-A2.1sup + melanoma cell line BLM, which lacks *gp100* expression and is resistant to lysis, becomes susceptible after transfection of *gp100* cDNA. Finally, HLA-A2.1sup + normal melanocytes are lysed by TIL 1200. These data demonstrate that the melanocyte differentiation antigen *gp100* can be recognized in the context of HLA-A2.1 by CTL from a melanoma patient. *Gp100* may therefore constitute a useful target for specific immunotherapy against melanoma, provided that no unacceptable cytotoxicity towards normal tissue is observed.

DRUG DESCRIPTORS:
**differentiation antigen*--endogenous compound--ec
MEDICAL DESCRIPTORS:
*melanoma cell; *tumor associated leukocyte
animal cell; antigen expression; antigen recognition; article; controlled study; cytolysis; dna transfection; *human*; *human cell*; nonhuman; priority journal
SECTION HEADINGS:
  016 Cancer
  026 Immunology, Serology and Transplantation
?ds

Set	Items	Description
S1	2	HUMAN DIFFERENTIATION ANTIGEN
S2	1	RD (unique items)
S3	0	S2 AND GP75
S4	0	HUMAN MELANOCYTE? AND GP75
S5	671	GP75
S6	0	S5 AND HUMAN DIFFENTIATION ANTIGEN?
S7	1795	GP100
S8	505	RD (unique items)
S9	0	S8 AND DIFFENTIATION ANTIGEN?
S10	671	GP75
S11	58	TRP-2
S12	27	RD (unique items)
S13	0	HUMAN PROSTATE ANTIGEN
S14	1030	PSMA
S15	400	RD (unique items)
S16	84	INSECT CELL LINE?
S17	42	RD (unique items)
S18	0	S17 AND S8
S19	0	S17 AND S12
S20	0	S17 AND S15
S21	0	S8 AND SF9 CELLS
S22	0	S8 AND SPODOPTERA FRUGIPERDA
S23	113	SPODOPTERA FRUGIPERDA
S24	108	RD (unique items)
S25	0	S24 AND GP75
S26	0	S24 AND HUMAN DIFFERENTIATION ANTIGEN
S27	0	HUMAN MELANOCYTES AND GP75
S28	211	MELANOCYTES AND GP75
S29	83	RD (unique items)
S30	0	S29 AND INSECT CELL LINE?
S31	1	S29 AND SF9
S32	0	S24 AND GP100
S33	0	S24 AND TRP-2

```
S34          0   S24 AND PSM
S35          0   S24 AND HUMAN PROSTATE ANTIGEN
S36          0   NON-HUMAN CELL LINE
S37          0   HUMAN DIFFENTIATION ANTIGEN
S38       1396   DIFFERENTIATION ANTIGEN
S39        997   S38 AND HUMAN
S40        703   RD (unique items)
S41          2   S40 AND GP75
S42          2   RD (unique items)
S43          9   S40 AND GP100
S44          9   RD (unique items)
?s s40 and trp-2
              703  S40
               58  TRP-2
     S45        0  S40 AND TRP-2
?s s40 and prostate specific membrane antigen
              703  S40
              286  PROSTATE SPECIFIC MEMBRANE ANTIGEN
     S46        0  S40 AND PROSTATE SPECIFIC MEMBRANE ANTIGEN
?s s40 and psma
              703  S40
             1030  PSMA
     S47        1  S40 AND PSMA
?t s47/5/a;;
>>>'A' not recognized as item list
?t s47/5/all

 47/5/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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11414319   BIOSIS NO.: 199800195651
Autoantibodies to *PSMA* in patients with early stage CaP.
AUTHOR: Culley D A(a); Fair W R; Heston W D; Wise G J(a); Gregor P D
AUTHOR ADDRESS: (a)Maimonides Med. Cent., Brooklyn, NY 11219**USA
JOURNAL: Proceedings of the American Association for Cancer Research Annual
Meeting  39p260 March, 1998
CONFERENCE/MEETING: 89th Annual Meeting of the American Association for
Cancer Research  New Orleans, Louisiana, USA  March 28-April 1, 1998
SPONSOR: American Association for Cancer Research
ISSN: 0197-016X
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
  MAJOR CONCEPTS: Clinical Chemistry (Allied Medical Sciences); Oncology (
    *Human* Medicine, Medical Sciences)
  BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata,
    Animalia
  ORGANISMS: *human* (Hominidae)--patient;  LNCaP (Hominidae
  BIOSYSTEMATIC CLASSIFICATION (SUPER TAXA): Animals; Chordates; Humans;
    Mammals; Primates; Vertebrates
  DISEASES: prostate cancer--neoplastic disease, reproductive system
    disease/male, urologic disease
  CHEMICALS & BIOCHEMICALS:   autoantibodies;  *PSMA*--*differentiation
    antigen*
  MISCELLANEOUS TERMS:   Meeting Abstract
CONCEPT CODES:
  24006   Neoplasms and Neoplastic Agents-Biochemistry
  16506   Reproductive System-Pathology
  34508   Immunology and Immunochemistry-Immunopathology, Tissue Immunology
  00520   General Biology-Symposia, Transactions and Proceedings of
            Conferences, Congresses, Review Annuals
BIOSYSTEMATIC CODES:
  86215   Hominidae
?ds

Set     Items   Description
```

```
S1          2   HUMAN DIFFENTIATION ANTIGEN
S2          1   RD (unique items)
S3          0   S2 AND GP75
S4          0   HUMAN MELANOCYTE? AND GP75
S5        671   GP75
S6          0   S5 AND HUMAN DIFFENTIATION ANTIGEN?
S7       1795   GP100
S8        505   RD (unique items)
S9          0   S8 AND DIFFENTIATION ANTIGEN?
S10       671   GP75
S11        58   TRP-2
S12        27   RD (unique items)
S13         0   HUMAN PROSTATE ANTIGEN
S14      1030   PSMA
S15       400   RD (unique items)
S16        84   INSECT CELL LINE?
S17        42   RD (unique items)
S18         0   S17 AND S8
S19         0   S17 AND S12
S20         0   S17 AND S15
S21         0   S8 AND SF9 CELLS
S22         0   S8 AND SPODOPTERA FRUGIPERDA
S23       113   SPODOPTERA FRUGIPERDA
S24       108   RD (unique items)
S25         0   S24 AND GP75
S26         0   S24 AND HUMAN DIFFERENTIATION ANTIGEN
S27         0   HUMAN MELANOCYTES AND GP75
S28       211   MELANOCYTES AND GP75
S29        83   RD (unique items)
S30         0   S29 AND INSECT CELL LINE?
S31         1   S29 AND SF9
S32         0   S24 AND GP100
S33         0   S24 AND TRP-2
S34         0   S24 AND PSMA
S35         0   S24 AND HUMAN PROSTATE ANTIGEN
S36         0   NON-HUMAN CELL LINE
S37         0   HUMAN DIFFENTIATION ANTIGEN
S38      1396   DIFFERENTIATION ANTIGEN
S39       997   S38 AND HUMAN
S40       703   RD (unique items)
S41         2   S40 AND GP75
S42         2   RD (unique items)
S43         9   S40 AND GP100
S44         9   RD (unique items)
S45         0   S40 AND TRP-2
S46         0   S40 AND PROSTATE SPECIFIC MEMBRANE ANTIGEN
S47         1   S40 AND PSMA
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